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IN
LEUKORRHEA
of Vaginal Origin TRICHOMONAD
INFECTION is probably the most common cause.[1]

[1]H. E. Schmitz, Medical Clinics of North America 27:43, Jan. 1943.

EFFECTIVE THERAPY
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[1]H. E. Schmitz, Medical Clinics of North America 27:43, Jan. 1943.

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Medical
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American Journal of Obstetrics and Gynecology

VOL. 49 JANUARY, 1945 No. 1

American Gynecological Society

Sixty-Eighth Annual Meeting, June 19 to 21, 1944

(Concluded)

AN INJECTION STUDY OF UTERINE BLOOD VESSELS*

ROBERT L. FAULKNER, M.D., CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, University Hospitals and Western Reserve Medical School)

INJECTION studies of the blood vessels of the uterus are not new. Sampson[1] in 1913, injected the vessels of the surgical specimen with gelatin and studied the vascular pattern in cross sections and radiograpically. He learned that the uterine veins contain no valves and are injectable. Since then the *arteries,* particularly, of the myometrium and endometrium have been studied by Barthelmez[2] from 1930 to 1941, by Jones and Brewer[3] in 1939, and others. In the monkey, Daron[4] in 1936, made a valuable contribution to our knowledge of the arteries of the endometrium by injecting mercuric sulfide into the vascular system during anesthesia. By immediately freezing the uterus in situ upon opening the abdomen, it was possible to study the vessels of the endometrium practically as they exist during life.

While injecting the arteries and veins of the myomatous uterus[5] with synthetic liquid latex, or Neoprene, it became apparent that good gross injections of the intrinsic vessels of the uterus were obtained. Therefore, injections were carried out on uteri removed for one cause or another at different phases of the menstrual cycle and on some bleeding uteri, especially those which contained only small or no demonstrable myomas. Over fifty specimens have now been injected for the study of the intrinsic vessels.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

Neoprene as an injection compound is easy to use, and this is important for the routine injection of suitable surgical specimens. It needs only to be filtered to be ready to use which is quite different from the commonly used gelatin which has to be prepared, kept free from mold, melted each time for use, and necessitates warming and chilling of the specimen before and after injection.

Injection of the blood vessels in a uterus of normal size is more difficult than the injection of those of a uterus containing myomas. There are two reasons for this: 1. The uterine vessels are smaller and less easily cannulated for injection; 2. The injection necessarily is the injection of end arteries and their emptying veins instead of the injection of a vascular arc as in most myomas.

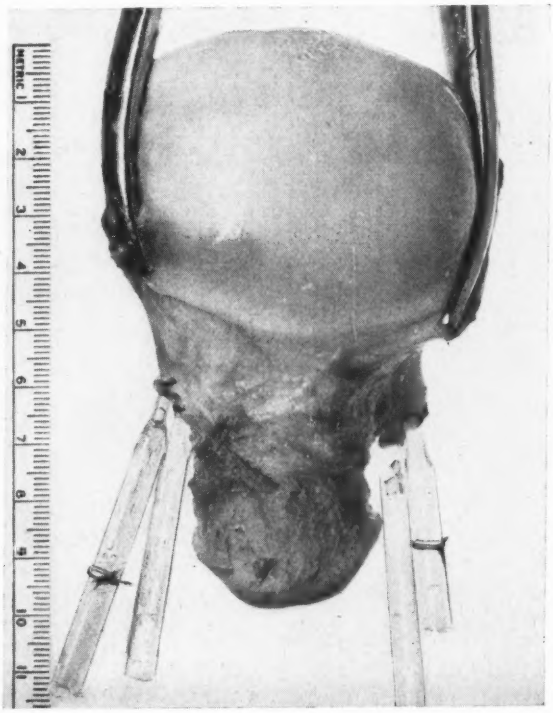

Fig. 1.—Uterus ready for injection. Black threads are on the venous cannulas.

In this study the method of injection was standardized as rigidly as possible. Throughout, the washing of the specimen was done in the same manner, the injection pressures used were always the same, the time of injection postoperatively was always the same, and all injections were done at room temperature.

All patients whose uteri were utilized were personally interviewed and their menstrual dates and habits carefully tabulated with full notation, also, of age, parity, and of any recent abnormal bleeding. Since the great majority of the specimens were for technical reasons of satisfac-

tory injection removed personally, this was no cursory inquiry. Hysterectomy was done carefully without traction sutures or clamps when possible. In some instances, a single traction suture was placed through the vertex of the uterus but used as little as possible.

Injection Method

Small glass cannulas (Fig. 1) were inserted into both uterine arteries and veins of the freshly removed specimen and at low pressure the blood washed out by connection to the arterial cannulas with a minimum amount of normal salt solution to produce blanching of the specimen. The uterus was then covered and put in the refrigerator over night, all leaking vessels having been ligated. Injection was done the next day, or twenty-four hours after removal of the uterus. All gross edema produced by the washing had by that time disappeared.

Fig. 2.—Corrosion cast of uterus showing black venous mass and uterine arteries with arcuate branches. Uterine veins cut away. Fundal branch toward top on either side. (From Am. J. Obst. & Gynec. 47: 185-197, 1944.)

Two forms of synthetic liquid latex were used: 1. A red suspension for arteries with a granule size of about 0.4 microns; 2. The other, a suspension containing a blue-black pigment for veins with a granule size of about 2 microns. The exact pigments contained in these preparations are not known, since they are proprietary injection compounds.* Lieb[6] found that they are satisfactory in obtaining a high percentage of glomerular injections in the kidney, and that in a general way, the granules go over into but not through the capillary bed.

On being brought back to room temperature, the arteries were injected with red neoprene from a simple pressure bottle set between 180 and 200 mm. of mercury. When the arteries were filled, there was no further flow. Black neoprene was then introduced into the veins at

*American Anode Inc., Akron, Ohio.

a pressure of 160 mm. of mercury. Filling of the veins produced a tense, swollen, and uniformly black uterus. Gentle massage of the specimen was carried out during venous injection to fill all the sinusoids. After removal of the cannulas, the vessels were tied and the specimen placed in 5 per cent formaldehyde strongly acidified with acetic acid. Any acid promptly sets this injection compound.

After thorough fixation, the uterus was bisected longitudinally and anteroposteriorly with a long sharp knife.

Neoprene lends itself to the preparation of multicolored corrosion specimens (Fig. 2). This preparation is made by eating off all the flesh with commercial hydrochloric acid leaving only the injected cast of

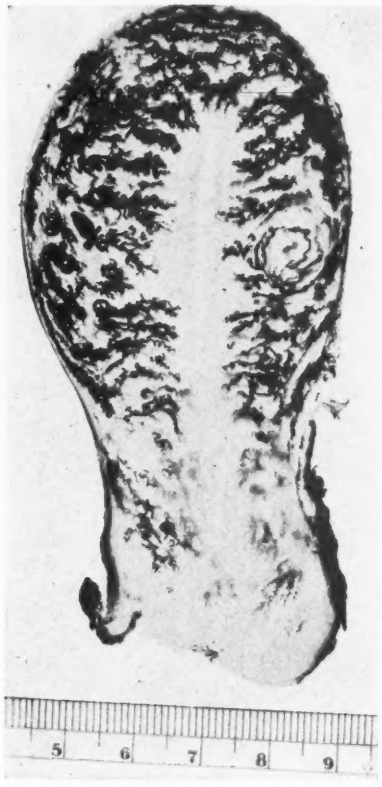

Fig. 3.—Arterial pattern of uterus. Spalteholz cleared preparation. One small myoma in uterine wall. Cervix does not inject in a surgical specimen. (From AM. J. OBST. & GYNEC. 47: 185-197, 1944.)

the circulation. The cervix does not inject in a surgical specimen because its vessels are stripped off during removal of the uterus. The uterine arteries with their arcuate branches to the front and back of the uterus are obvious. The uterine veins have been cut away. A large branch of the uterine artery usually goes on over the fundus. The large bulk of the venous sinusoids which retain the contour and almost the complete size of the original specimen is evident.

The internal arterial pattern of the uterus may be seen in Spalteholz cleared specimens. The black pigment in neoprene will stand the clearing process in benzol and wintergreen oil (Fig. 3). The rich peripheral circulation of the uterus may be seen. Through these anastomoses one

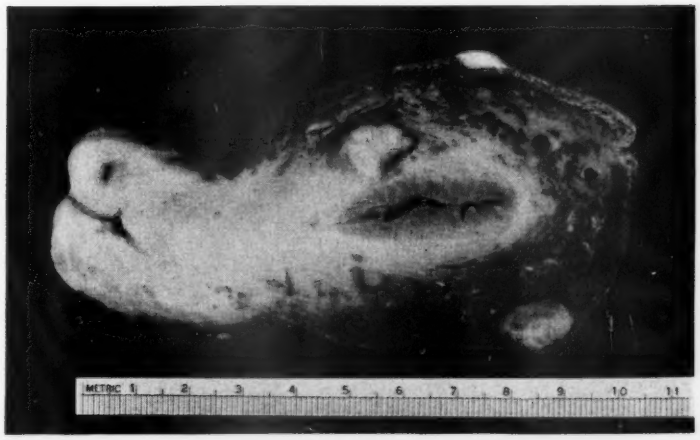

Fig. 4.

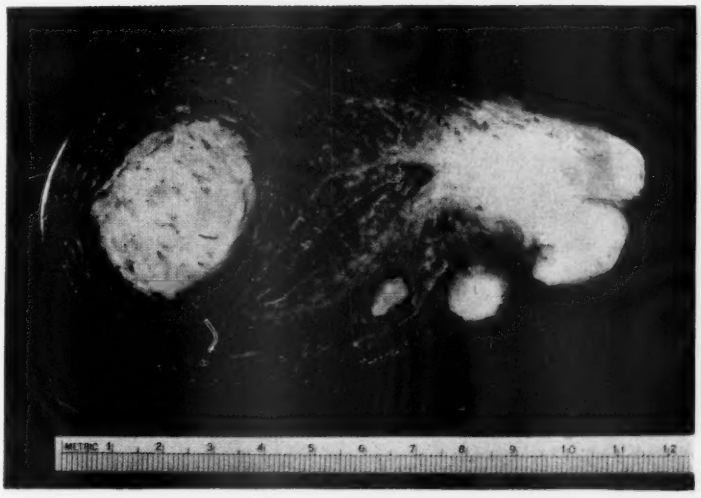

Fig. 7

Fig. 4.—Injection of uterus removed seventh day of menstrual cycle. Aged 45. Para iii. Small myomas. Periods normal. Zone of uninjectability about uterine cavity.

Fig. 7.—Beginning of menstrual flow. Aged 38. Para i. Escape of venous injection mass into uterine cavity.

uterine artery communicates so freely with the other. The pattern of the radial arteries all pointing toward the uterine cavity is always almost diagrammatic unless distorted by myomas.

Neoprene in common with other colloids does not penetrate the terminal branches of the radial arteries. They are filled normally only up into the inner quarter of the myometrium. The endometrium is not injected. Daron believed that in addition to a contraction cone active during life, that there is also an anatomical narrowness of arteries in the submucosal zone before they enlarge again to those of the endometrium. Injection experience with neoprene would seem to confirm this opinion.

Fig. 5.—Fourteenth day of cycle. Aged 28. Para i. Slightly more injectability of submucosal zone.

Therefore, it is particularly the veins of the uterus as they may be an index to blood supply that are studied with neoprene. It is true that the arteries of the endometrium seem to be important in explaining the now well-known rhythmic blushing and blanching of the endometrium in menstruation, and also probably explains its shedding, but it has never been proved successfully that the source of menstrual blood may not be venous reflux in large measure.

Sampson observed in many specimens an uninjectable zone about the uterine cavity except in uteri which were bleeding, about to bleed, or had recently been bleeding. In specimens carefully arranged as to menstrual dates and not containing myomas which might interfere with the picture, it would seem that this zone of uninjectability is an almost constant finding postmenstrually up to approximately the time of ovulation (Figs. 4 and 5). After that there is increasing venous in-

jectability of this area with uniform and almost complete entrance of the injection mass as menstruation approaches (Figs. 6 and 7).

Near the end of menstruation (Fig. 8) in a limited number of specimens injected at this time, there is a return of the uninjectable zone except opposite areas where shedding of the endometrium is incomplete. The same picture of patchy or irregular injectability is seen in other uteri with abnormal bleeding (Fig. 9).

With the aid of Dr. Normand L. Hoerr, Professor of Anatomy, efforts were made to prove the postmenstrual ischemic zone an injection artefact.

Fig. 6.—Twenty-fifth day of cycle. Aged 30. Para i. Uniform injectability of submucosal zone.

Obviously all tissues, particularly veins and smooth muscle, should be devitalized after twenty-four hours. To make sure, however, that the time of injection made no difference, several specimens were injected as late as four or five days after operation. If the uterus was postmenstrual, the same uninjectable zone was observed. Nitrite solutions were perfused through the arteries. Specimens so treated did not seem to be altered in their injectability. The possibility of connective tissue swelling during the washing process with clamping off of veins was considered. Several specimens were injected without washing. These were the poorest of all. An occasional specimen was injected only through the arteries in an effort to see if veins in the uninjectable zone would be filled with blood. No filling of the veins by this method was proved. Briefly, nothing to date has succeeded in altering

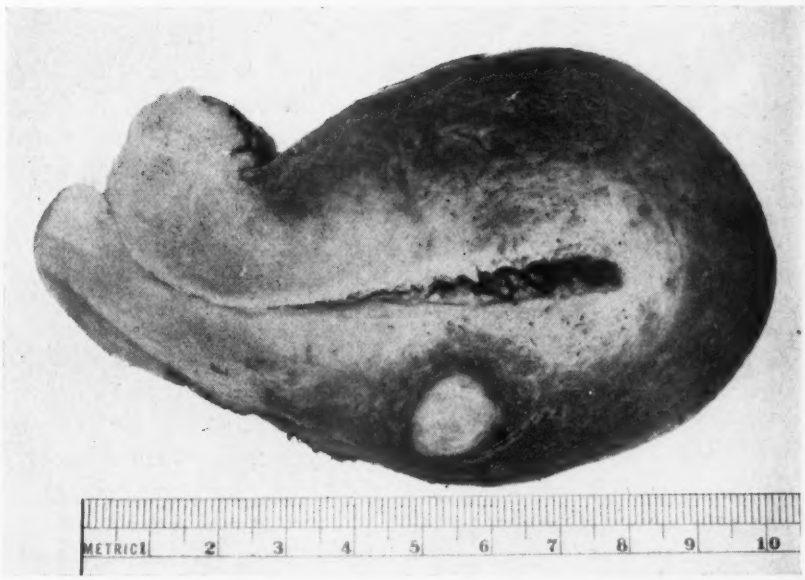

Fig. 8.—Third day of usual four-day period. Aged 44. Para ii. Return of uninjectable zone except at points opposite small myoma where endometrium remains to be shed.

Fig. 9.—Uterus removed twelfth day of bleeding. Aged 32. Para 0. Escape of venous mass through middle portion of uterus with less injectability in vertex and lower uterine cavity.

the general picture of uninjectability in the submucosa of the endometrium.

This region was studied with special stains microscopically. There is no obvious increase in connective tissue postmenstrually that can be seen in Masson's stain. The only thing that is regularly apparent is a definite increased compactness of the musculature in this region. Premenstrually, the zone becomes loose and spongy and is injectable with the greatest of ease.

Summary and Conclusions

In the uterus carefully removed at surgical operation and the vessels injected with synthetic liquid latex with a standardized technique, the presence under ordinary conditions postmenstrually of an uninjectable zone surrounding the uterine cavity as observed by Sampson over thirty years ago is observed again. Attempts were made without success to prove this zone an injection artefact. Morphologically, no change in the uterine wall in this zone was recognized except an increased compactness of uterine musculature. This region, after the period, resembles the myoma somewhat in its manner of injection. In the premenstrual uterus, this zone becomes spongy and is injectable. In some specimens with irregular uterine bleeding, there may not be uniform injectability of the submucosa but a localized entrance of the injection mass here and there to the endometrium.

Since the type of endometrium has been rather conclusively found to have little connection with the fact of uterine bleeding, it would seem a legitimate effort to learn more if possible of the physiology of the uninjectable zone surrounding the uterine cavity.

Grateful acknowledgment is made of the technical advice of Miss E. Lieb in making these injections, to Dr. Normand L. Hoerr for critical analysis of the material, and to the Department of Pathology for the colored illlustrations.

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Discussion

DR. WILLIAM E. STUDDIFORD, New York, N. Y.—Dr. Faulkner has presented a simple and efficient method of demonstrating the intrinsic arterial and venous systems of the uterus. Synthetic latex appears to have definite advantages over the more difficult gelatin mass formerly utilized in such studies.

His study of relatively normal uteri injected in this fashion has yielded results, which conform closely with those obtained by Sampson in a report presented before this Society over thirty years ago. In the older report the same zone of low injectability was noted adjacent to the endometrium, although the alteration of this zone in the premenstrual phases was not stressed. Both of these reports have

suggested that this zone of the myometrium plays an important part in regulating the quantity of the menstrual flow.

This study strikes at the fundamentals of a most bothersome clinical problem. While much has been learned of the physiology of the menstrual cycle in recent years, particularly in regard to the growth and development of the endometrium under hormonal stimulation, and its breakdown following the withdrawal of such stimulation, this knowledge has proved to be of no value in the treatment of the patient who suffers from prolonged and profuse menstruation from a uterus which otherwise appears quite normal.

Studies of the endometrium obtained from these patients usually show no pathologic change. It is reasonable to suppose that the fundamental defect in many of them lies in the myometrium. Dr. Faulkner has demonstrated the area in which this defect may lie. Further studies of the myometrial relationship to menstrual bleeding may yield more constructive results.

Has Dr. Faulkner made any injection studies in uteri containing an early pregnancy? In several such specimens, containing pregnancies ranging from twenty-six to forty-four days of age, sections of the myometrium showed a pronounced zone of edema and vasodilatation beneath the serosa in the area supplied by the peripheral branches of the arcuate arteries. The changes suggest a zone of pronounced vascular disturbance in the outer third of the myometrium during the early months of pregnancy. They are not present in the inner two-thirds of the myometrium.

DR. FAULKNER (closing).—I desire to state that up to the present time no studies on pregnant uteri have been made.

RELATIONSHIP OF GLYCOGEN TO PROBLEMS OF STERILITY AND OVULAR LIFE*

EDWARD C. HUGHES, M.D., SYRACUSE, N. Y.

THE process of ovulation, fertilization and housing of the growing embryo is the important biologic function of the female species. The satisfactory maintenance of these processes depends upon the intricate function of the various endocrine glands, the metabolism of essential materials, and the effect of hormones and enzymes. There is no doubt that nature's most complex problem is to furnish ever increasing amounts of foodstuff, not only to the sperm after it enters the female generative tract, but particularly to the ovum after it leaves the Graafian follicle, is fertilized and implants itself on the surface of the endometrium. Essential nutriments for these vital cells include many substances, particularly oxygen and carbohydrates. Glucose has been found to increase in amount in the early fertilized avian egg and the eggs of lower mammals. An increased utilization of this sugar in human beings may be a phylogenetic remnant from these lower forms. The problem of providing these materials is difficult during the early period of implantation, before the embryo establishes a close intimacy with the mother by placental formation and growth. It is during these days of nidation that many observers have stated that the trophoblast lives almost exclusively on glucose and oxygen. This fact probably explains the presence of glycogen, the storage product of glucose, in such abundance in all parts of the reproductive tract, and leads to this discussion concerning the importance of this material to satisfactory nidation or ovular life.

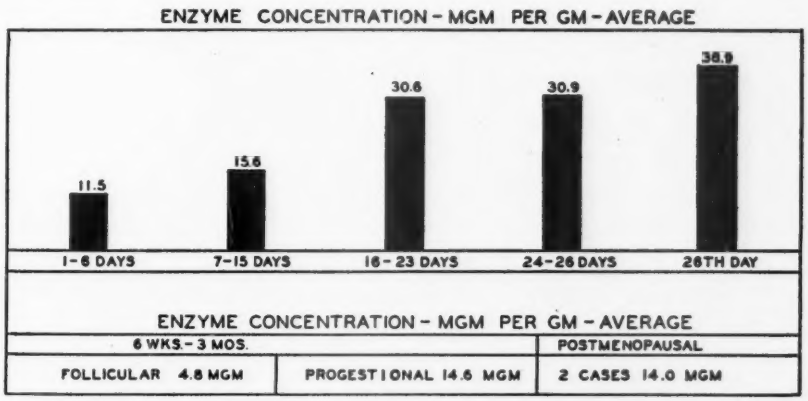
Distribution of Glycogen in the Reproductive Tract

In normal individuals, glycogen seems to be present in all the tissues with which the ovum comes in contact. It is found in the cells of the cumulus oophorus while the egg is still in the Graafian follicle. It is secreted by the epithelial cells of the Fallopian tubes. It is produced in the endometrium of the uterus in increasing amounts after ovulation and fertilization. It is during the early days of implantation that some intermediate substance of low molecular weight such as glucose and oxygen must be provided by the endometrial glands to furnish nutriment which is easily and readily assimilated. However, inasmuch as glucose cannot be stored as such, it must be derived from glycogen. One can thus feel that glycogen is stored in the endome-

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

trium in anticipation of fertilization whereby in the usual chemical manner, sugar is made available for ovular usage. This chemical process is probably similar to that which goes on in the other organs of the body where conversion to glycogen and storage occurs. This glycogenesis and glycogenolysis must go on in the endometrium in the same manner, involving the presence of an enzyme or possibly by enzymes.

The endometrium has been examined for enzymes previously by Reynolds and others. They have concluded that there perhaps are several present. In this study, sections of endometria have been removed by the biopsy curette, and have been studied for the presence of an enzyme responsible for the glycogen hydrolysis. The subjects from whom these biopsies were removed were fifty normal women, who had given normal menstrual histories. The method, as worked out by Dr. Robert K. Brewer, Professor of Chemistry, College of Medicine, Syracuse University, is as follows:



Method of Enzyme Determination

Samples of endometrial tissue removed by curette were carefully wiped with filter paper, in an attempt to remove as much as possible of the adherent mucus, and then the samples were transferred to weighed tubes and again weighed. A mixture of 25 per cent glycerin in normal saline at pH 5.0 was added, and the sample extracted for 24 hours at 38° C. with occasional shaking. Aliquot portions of the extract were treated with ten volumes of 95 per cent alcohol, and the precipitated enzyme thrown down in a centrifuge tube. After thorough draining, the enzyme was dissolved in a pure glycogen solution and incubated at 38° C. for 24 hours. The reducing substance was then determined by Benedict's blood sugar method, calculated as glucose, and reported as milligrams of reducing sugar per gram of tissue. Blanks were run on all reagents used as well as on heated controls to give proof that the reducing substance formed was the result of enzyme action on the pure glycogen in solution.

The only claim advanced for the value of the figures obtained is that by doing 147 analyses by the same method, using the same reagents, we obtained results which we consider to be of value for comparative purposes.

The average amounts of enzyme seem to vary according to the menstrual cycle. These are illustrated in the following:

Days	1 to 6	7 to 15	16 to 23	24 to 26	26	
	11.5	15.6	30.6	30.9	36.9	mg. per gram

It was also observed that as far as we could determine, the hydrolysis of glycogen by this enzyme did not pass to glucose but to a di- or trisaccharide. The enzyme was also found in larger amounts in mucous secretion of the endometrium than in the tissue itself. It was interesting to note that determinations made upon women in the six-week to three-month period post partum, and postmenopausal women were definitely lower than normal. These averages were as follows:

Sixth week to three months, in the follicular phase—4.8 mg.
Progestional phase—14.6 mg.
Postmenstrual women—14.0 mg.

Although it seemed as if the enzyme production varied quantitatively with the phase of the cycle, it was found necessary that the endometrium be studied carefully to correlate the amounts of enzyme with the location and quantities of glycogen present in the various phases of the cycle. Therefore, each biopsy of the endometrium that was obtained for enzyme determination was also stained for glycogen. These sections were stained by Best carmine technique.

The Distribution of Glycogen in the Endometrium

The distribution of glycogen in the endometrium seemed to be important, and seemed to follow a constant sequence of events in the normal cases, according to the phase of the cycle. Glucose was brought to stroma of the endometrium by the arterioles, where dehydration to glycogen apparently started. This occurred about the end of the first week of the follicular phase, and the glycogen appeared as small granules sparsely scattered about the base of the endometrial glands. (Fig. 1.) Dehydration continued during the second week, followed by beginning accumulation at the base of the glandular epithelial cells. (Fig. 2.) The nuclei of these cells were pushed upward to the mid-zone of the cell. (Fig. 3.) At the end of the second week, glycogen continued to be stored in granular form until after ovulation, when it was released from the epithelial cells into the lumen of the glands and onto the surface of the endometrium. (Fig. 4.) The periphery of the epithelial cells became frayed and ragged after glycogen was released. The glycogen was then hydrolized by enzymatic action into a reducing sugar.

I feel that this distribution of glycogen in the endometrium during its various cyclic phases is an important occurrence, similar to the glandular and stromal changes. Also the relation of the enzyme concentration to the glycogen distribution is necessary, in order to have satisfactory metabolism of this material. Deviations of these correlations generally denoted some hormonal or glandular insufficiency directly related to sterility problems and ovular changes. To substantiate these opinions, I would like to discuss the relationship of these things to problems of sterility and spontaneous abortion.

Relationship of Glycogen and Enzyme Concentration to Sterility

In certain types of sterility conditions, these normal findings in the endometrium were not observed. This was noted in the study of 140 women who presented themselves for sterility. These patients were studied completely and thoroughly. Endometrial biopsies were obtained upon the twenty-sixth day of the cycle, and were analyzed carefully in each case. The endometria of 40 of these women were also tested for enzyme concentration. The type of sterility was classified by the type of endometrium found. The patients fell into three groups according to this classification.

GROUP I

66 PATIENTS — AVE. AGE 30 YRS

ENDOMETRIUM		ENZYME CONC.	MENSTRUAL HIST		LOCAL PATHOLOGY		BMR	MALE
PHASE	GLYCOGEN	36.9 MGM/GM.			UTERUS - NORMAL	47		
					RETRO	15	ABOVE,	
SECRETRY	NORMAL	30.5	28 DAYS	51	STENOSIS	2	34	
66	66				TUMORS	2		
			24-28 DAYS	2			NORMAL,	
					OVARIES - TUMORS	8	4	
			28-35 DAYS	13				10
					TUBES - CLOSURE	17	BELOW, 22	
					CERVICAL & VAGINAL	10		
		NORMAL 17 PATIENTS					NOT DONE 6	

RESULTS - 26 PREGNANCIES

1. 11 PREGNANCIES AFTER CORRECTION OF RETROVERSION
2. 2 " " DILATATION OF CERVICAL STENOSIS.
3. 5 " " TUBAL PATENCY TESTS
4. 8 " " LOCAL TREATMENT FOR EROSION AND VAGINAL DISCHARGE

The first group consisted of 66 women, who were found to have a normal endometrial pattern, with normal distribution and amount of glycogen. (Fig. 5.) The cause of the sterility was from some pelvic pathology, or male impotency. After correction of the local difficulties, pregnancy resulted in 26 patients. The following treatments were carried out:

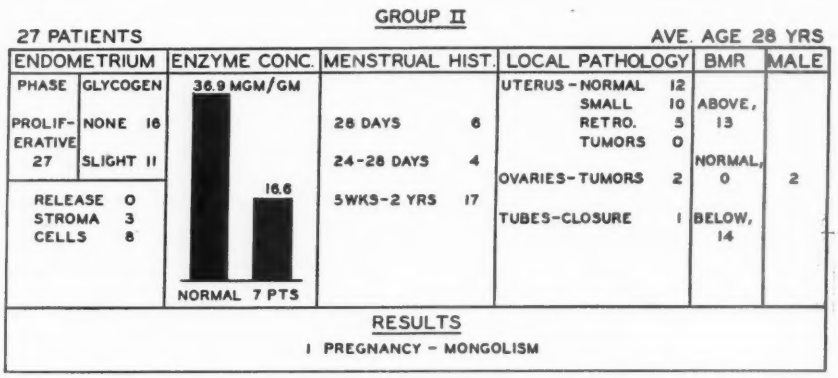
1. Retroversion corrected with pessary in 15 cases, followed by pregnancy in 11 patients.
2. Cervical erosion and stenosis were treated in 2 cases with resulting pregnancies.

3. Tubal patency tests were done on all patients. Seventeen patients were found to have tubal obstruction. Five of these patients conceived after treatment.

4. Eight patients conceived after treatment of other conditions that were present, such as erosion of the cervix and trichimonas vaginitis.

Seventeen patients of this group had enzyme determinations done upon the endometrium. The average was 30.5 mg. per gram, which is considered normal.

The second group of patients consisted of 27 women, in whom the endometrium failed to proceed farther than the proliferative phase, and the glycogen was absent or present in only small quantities. (Fig. 6.) Enzyme determination in 7 patients was under normal, averaging 16.4 mg. per gram. These patients were treated with all the various gonad-stimulating hormones. The results were unsatisfactory. Ovulation and pregnancy occurred in only 1 patient, the fetus was born a Mongolian idiot.



The third group, consisting of 47 patients did not seem to present a normal endometrial pattern, the glycogen distribution was irregular, and the enzyme content was markedly below normal. The phase of the cycle proceeded to the early secretory phase in 31 patients, but did not correspond to the twenty-sixth day of the cycle. (Fig. 7.) The glycogen was not released from the cells in some cases, and in others was only partially metabolized. In the other 16 patients, the endometrium was spotty, in some areas progressing to the early secretory, and in other portions to the late secretory phase. The glycogen was partly released in some, or retained in the stroma about the glands in others. (Fig. 8.) The enzyme production was again below par, averaging 15.5 mg. per gram in 16 patients.

This group, inasmuch as they showed comparatively little pathologic findings in the pelvic organs, but showed disturbed menstrual function and abnormal endometrial patterns, was classified as endocrine problems, and was treated with this in mind with the following results:

1. Eight patients in the lower level of metabolism were treated with thyroid extract, and 4 pregnancies resulted.

Fig. 1.—Early proliferative phase with several granules of glycogen staining red at base of the epithelial cells.

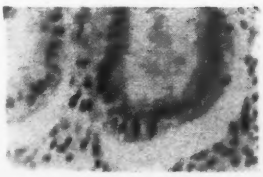


Fig. 2.—Nuclei pushed to midportion of cell by glycogen granules.

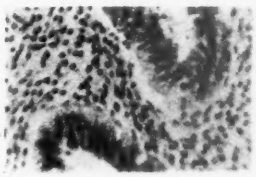


Fig. 3.—Early secretory phase with some glycogen release into lumen of gland.

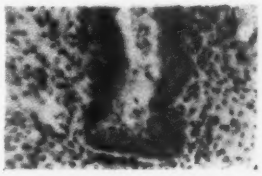


Fig. 4.—Glycogen granules released into lumen of gland. Late secretory phase.

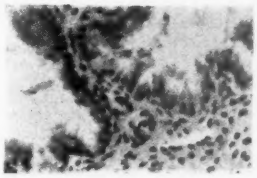


Fig. 5.—Normal endometrium with glycogen release in secretory phase.

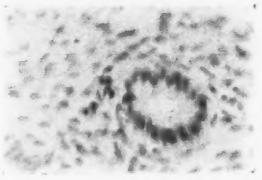


Fig. 6.—Endometrium remains in the proliferative phase without glycogen.

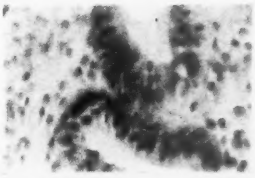


Fig. 7.—Late proliferative phase with partial glycogen metabolism.

Fig. 8.—Glycogen retained in the stroma. Glandular epithelium is devoid of glycogen. Poor metabolism of glycogen.

Fig. 9.—Biopsy taken after pregnancy while ovum is still in tube. Large amount of glycogen in lumen of glands.

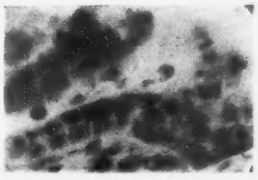


Fig. 10.—Pregnancy—large amount of glycogen.

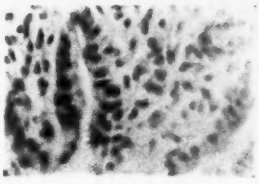


Fig. 11.—Endometrial gland with glycogen present in glandular epithelium. Decidual cells with glycogen granules.

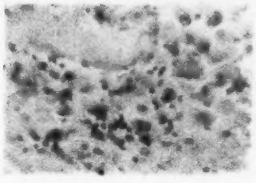


Fig. 12.—Chorionic villus surrounded by decidual cells containing glycogen granules.

2. Sixteen patients were treated with an estrogen, and 10 pregnancies resulted.

3. Sixteen patients were treated with a gonadotropic hormone, and 6 pregnancies resulted.

4. Two patients conceived following the endometrial biopsy, and 2 conceived without treatment.

GROUP III

47 PATIENTS — AVE AGE 29 YRS

ENDOMETRIUM		ENZYME CONC.	MENSTRUAL HIST.		LOCAL PATHOLOGY		BMR	MALE
PHASE	GLYCOGEN	38.9 MGM/GM			UTERUS-NORMAL	26		
SECRET'RY 31	RELEASE 9		28 DAYS	15	SMALL	6	ABOVE, 22	
					RETRO	14		
IRREG SECRET'RY 16	STROMA 9		21-28 DAYS	4	TUMORS	1	NORMAL, 0	3
	SI RELEASE 29	15.5	28-6 MOS.	28	OVARIES-NORMAL	47		
			SCANTY 2-3 DA.	21	TUBES - NORMAL	47	BELOW, 25	
			NORMAL 4-5 DA.	16				
			MORE 5-10 DAYS	10				
		NORMAL 16 PTS.						

RESULTS-24 PREGNANCIES

	THYROID	ESTROGEN	GONADOTROPHIC	NONE
PATIENTS TREATED	8	17	16	6
PREGNANCIES	4	10	6	4 (2 PTS AFTER BIOPSY)

The Relationship of Glycogen and Enzymes to Pregnancy and Spontaneous Abortion

While the metabolism of glycogen seems to be an integral part in the cyclic changes that occur in the endometrium in normal and abnormal cases, its continual and increased output seems particularly necessary after fertilization takes place.

Claude Bernard, in 1858, and later Chapman, found that glycogen was in abundance in the maternal portion of early placentas. Four endometrial biopsies obtained accidentally upon the twenty-sixth day of the cycle, after fertilization had occurred but while the ovum was still in the tube, revealed larger amounts of glycogen than usual in the epithelial cells and in the glands. (Figs. 9, 10.) Incidentally, these patients did not abort. Also, tissue removed for therapeutic abortion in the second month of pregnancy showed large granules of glycogen in the decidua and endometrial glands. (Figs. 11, 12.)

These demands for larger amounts of glycogen result in increased metabolism, involving more enzyme production, and greater supply of sugar to the endometrium. Failure of the endocrine system to provide this stimulation, with resulting lack of these materials ends in the death of the early embryo. It was interesting to note the frequency of spontaneous abortion in the three groups of patients just discussed. The incidence as obtained from their past histories was as follows: Fifteen women had a total of twenty-three miscarriages. The second group, where pregnancies were infrequent and enzyme con-

centration was low, five women had nine abortions. In the third group, in whom the glycogen distribution was abnormal, phase retarded and enzyme concentration low, twenty-six women had fifty-eight spontaneous abortions.

This would lead us to believe that when the glycogen metabolism is not complete, as shown in the third group of patients, the opportunities for ovum survival are not good. Microscopic studies were made upon the products of conception and curettings in some of these cases, and they showed early ovular death with necrosis and infiltration of leucocytes in the decidua.

INCIDENCE OF SPONTANEOUS ABORTION

	GROUP I, 66 PATIENTS	GROUP II, 27 PATIENTS	GROUP III, 47 PATIENTS
ENDOMETRIUM	NORMAL	ABNORMAL	ABNORMAL
ENZYME CONCENTRATN	30.5 MGM	16.6 MGM	15.5 MGM
SPONT ABORTION	15 WOMEN - TOTAL 23 26.6 %	5 WOMEN - TOTAL 9 18.5 %	26 WOMEN - TOTAL 58 55.3 %

Discussion

In discussing the importance of glycogen to these vital processes several opinions were formulated. Ovulation probably does not occur when the endometrium remains in the follicular phase, the glycogen is absent or diminished and the enzyme production low. This picture was exemplified in Group II. Opportunities for pregnancy in these individuals are few even after hormonal stimulation.

Individuals, in whom the endometrium proceeds to the progestational phase, possess relatively larger amounts of glycogen but still have a low enzyme output, conceive without difficulty; however, the chances of survival of the ovum are not good and spontaneous abortion results. These conditions were found in Group III. These women, however, were more amenable to treatment but the therapy should be instituted prior to pregnancy and during the early days of gestation. Ten patients in this series were treated as follows: Small doses of estrogen were given before pregnancy to improve glycogen and enzyme production as shown by endometrial biopsies and enzyme determination. After pregnancy occurred, combined treatment of small doses of estrogen and progestin were prescribed during the first trimester and early part of the second trimester. These women had never before carried beyond the fourth month, but after treatment proceeded uneventfully to term.

Summary

Several thoughts are brought to mind in attempting to summarize these findings.

1. A better understanding of the many chemical changes in the endometrium should be attempted.

2. Glycogen is an important material of the endometrium, and its metabolism is probably influenced by the ovarian hormones as previously described by Overhauser and Nelson.

3. Also, the glycolysis that occurs in this location may be associated with the metabolism of estrogen and progestin in the endometrium itself.

4. There has been no proof that the progestational increase in amounts of glycogen and its enzyme is not associated with a general bodily increase.

5. The satisfactory metabolism of glycogen is necessary for ovulation and ovular life.

I wish to express my gratitude to Dr. N. P. Sears who has studied and diagnosed each biopsy sample.

Discussion

DR. NATHAN P. SEARS, SYRACUSE, N. Y.—All of Dr. Hughes' material was sent to my laboratory and one technician prepared it. The glycogen stains were studied carefully and many types were tried before we were convinced of the properties of the stain. At first identical pieces of tissue were put through hematoxylin and eosin stains in addition to the glycogen-stained specimen. The slides were presented to me more or less as unknowns, so that I could identify the phase of the cycle and then follow the location of the glycogen granules in the tissue. I then went over the history of the case as found in the patient's record to look for any discrepancies from the normal. Some patients in the twenty-fifth or twenty-sixth day of the cycle showed some secretory areas highly developed and others poorly developed. The presence of glycogen coincided most of the time with the histology, but when there was a variation, the glycogen seemed to me more accurate. Dr. Hughes then took my reports without any comments on my part, except mention of the abnormalities, and studied the clinical factors along with the laboratory findings.

There is in this subject something of extreme general interest. We are at present in a phase in which we try to explain most functional derangements on a hormone basis, but the hormones have not solved all of our problems. I wonder if we will not be able to use the concept here presented to determine why so many women have long periods of amenorrhea, and others irregular and profuse bleeding without showing any pathological lesion, nor responding to hormone therapy. Some new studies on the metabolism of the sugars may be evolved which will make it possible to change the sugar metabolism and thereby bring about a better glycogen balance which, in turn, will correct the physiology of the childbearing organs.

DR. EMIL NOVAK, BALTIMORE, MD.—We may now have to add another to the already numerous procedures often indicated in the study of sterility. The fact that glycogen undoubtedly plays an important part in the nutrition of the egg before it implants itself in the endometrium makes it seem probable that it plays a similar role in the early postnidation phase. After the egg is thrown off from the ovary, a considerable number of days elapse before it takes root in the uterus. During this time, this single cell floats in space, so to speak, and yet if fertilized it lives and thrives. Where does it get its nutrition?

When it leaves the ovary it, figuratively speaking, packs a lunch box for itself, since with it go many adhering cells of the cumulus oophorus which will be assimilated by the egg, whose cytoplasm probably contains only a minimum of

nutritional granules in itself. During its transit through the tube, the egg may receive additional nutriment from the glycogen-rich cytoplasmic and nuclear extrusion of the secretory cells of the tube wall.

Even when it reaches the uterus, it does not at once implant itself, and during this loitering phase, it is further nourished by the glycogen-rich secretion of the uterine glands. In some animals, like the horse, this secretion is almost milky in its nutritional value, and has indeed been spoken of as "uterine milk." Still later the egg, in the process of implantation, benevolently assimilates the cells of the endometrium before it finally taps the maternal vessels for a more permanent source of nutrition.

The maternal decidua likewise is rich in glycogen, and it would appear from the studies of Zondek, and those reported today by Dr. Hughes, that the presence of this glycogen is important and perhaps essential for the implantation of the egg. Zondek described a glycopenia of the endometrium as associated with some cases of sterility, even when the endometrium shows a typical progestational picture histologically.

In other words, it is hazardous here, as in so many other fields, to use mere morphological changes as a criterion of the functional status of a tissue. For example, even an actively mobile spermatozoon may be incapable of fertilizing an egg. Conversely, the mere fact that endometrial biopsy demonstrates that an egg has been thrown off does not justify us in assuming that the egg is a fertilizable one. To confuse the problem still more, we now must suspect that even if the egg is fertilized, it may meet with an unfavorable reception in the endometrium as a result of such factors as glycogen deficiency.

Since we know comparatively little as yet as to the endocrine or other mechanisms involved in these factors, we cannot attack them with any very intelligent corrective measures, but the mere recognition that they exist will help us to explain some of our sterility cases, and will spur investigators to further efforts to increase our knowledge on these points.

DR. KARL MARTZLOFF, PORTLAND, ORE.—I would like to ask Dr. Hughes just how he obtained his endometrial tissue for biopsy; whether samples were taken from the entire intrauterine cavity, or from just one or the other wall. It has been our experience that biopsies obtained from one point in the uterine cavity are an unreliable index as to the status of the endometrium, and that if one wishes to have a fair index it requires a sample from all walls of the cavity. We find that domestically manufactured carmine is an unsatisfactory substance and we have to use Grübler's carmine for our glycogen stains.

DR. HUGHES (closing).—Replying to Dr. Martzloff's question, we found it was necessary to take three strips at least from the internal surface of the uterus, generally starting from the fundus, coming down through the anterior wall, lateral wall and posterior wall. We found that there was more glycogen in the fundal portion than in the lower portion of the uterus, so that the picture evidently changes somewhat from the fundus to the internal os. We used an ordinary biopsy curette without the suction, for with the suction we found that we lost some material.

Many sections have to be restained. There is a new technique, but we still use carmine, for it gives a more satisfactory result than the old glycogen stain.

PELVIC LYMPHADENECTOMY IN THE TREATMENT OF CERVICAL CANCER*

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(From the Department of Obstetrics and Gynecology, University of California Medical School)

METASTASES in the regional pelvic lymph nodes have long constituted a stumbling block in the treatment of cervical cancer. In many instances, glandular involvement occurs only in association with extensive local growth, making a combination which spells doom for the patient. In other instances, regional node metastases exist even when the local growth is early enough to permit surgical eradication or destruction by radiation. It is in the latter group of cases that we are interested, for in them there exists at least the possibility of removing or destroying all the involved tissues. Forty odd years ago, the attempts to meet the problem were surgical; the regional glands were excised in the course of operations to remove the entire uterus, cervix, parametria, and upper vagina. The applicability of the surgical method was, however, limited by the operability of the local growth and by the high mortality entailed by such extensive procedures. It should be appreciated, of course, that operation was the *only* method of treatment available at that time, and that therefore as many cases as possible were subjected to the procedure. "Inoperable" meant actually impossible to remove. A high mortality naturally resulted from attempts to remove rather far advanced growths. As high voltage roentgen therapy reached an effective stage of development 15 years ago, the possibility of destroying cancer in the parametria and in the regional glands by this means moved to the fore. However, there still remained a group of cases in which the local cervical response to radiation promised much, yet death occurred soon after presumably because of the survival of cancer in the regional nodes. It appeared that metastatic cancer in lymph nodes was much more insensitive to radiation than the parent tumor, at least, it should be added, to the radiation available at that time. These considerations led the late Dr. Frederick Taussig to suggest a surgical resection of the regional pelvic lymph nodes as a supplement to radiation in the early inoperable group of cases.

His first operation was performed in October, 1930, and his last report, published in the Fall of 1943, gave the details of 175 such operations. Independently, at about the same time, Leveuf, in France, had a similar idea, and since then a small number of such operations

*Read at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

(Leveuf, Michel-Bechet) have been performed in that country. In 1936, Duncan reported three cases of lymphadenectomy and suggested the use of interstitial radon seeds and ligation of the uterine arteries as adjunct to the procedure. In 1935, being impressed by Taussig's reasoning, we at the University of California Hospital, started to perform this operation upon certain selected patients. A small series of cases has since been accumulated, upon which are based the results and impressions contained in this paper.

TABLE I. INCIDENCE OF GLANDULAR INVOLVEMENT (FROM THE LITERATURE)

AUTOPSY CASES	PER CENT	OPERATIVE CASES	PER CENT
Wagner	50	Kundrat (80 cases—serial sections)	32.5
Williams	72	Brunet (47 cases—serial sections)	51
Dittrich	40	Kermauner (73 cases—serial sections)	43.8
Blau	33	Sampson (19 cases—serial sections)	47
Schauta (50 cases, serial sections)	64	Bonney (500 cases)	40
Warren (1933)	63.7	Taussig (175 Stage II cases)	26.8
Behney (1933)		Baisch (52 cases—parametrium clinically free)	19.2
(Any metastatic lesion)		Leveuf and Godard (36 cases status unknown)	50
80 treated patients	21.2	Leidenius (21 cases—Wertheim)	28.6
86 untreated patients	44		
Morton (1935) (36 cases)	44.4		
Pearson (1936) (57 cases)	59		

SERIAL SECTION STUDIES

PARAMETRIUM INVOLVED		PARAMETRIUM FREE	
Schauta		Schauta (10 cases)	20.0
Brunet		Oehlecker (35 cases—collected, Schauta 10, Oehlecker 7, Baisch 18)	31.0
Baisch	Approximately		
Kermauner	50 per cent		
Kundrat		Kundrat (36 cases)	11.1
Sampson		Sampson (10 cases)	30.0

The Incidence of Gland Involvement

Of great importance in deciding the indications for such a procedure as lymphadenectomy is a knowledge of the incidence of glandular involvement, particularly in relation to the degree of advancement of the local growth. Unfortunately the literature does not contain a really satisfactory study of the incidence of glandular involvement. Most of the available figures were obtained shortly after the turn of the century and were derived from two main sources; from autopsy cases, and from cases in which the radical operation had been performed. In the autopsy cases the disease was advanced and terminal, and in many instances the results were unconfirmed microscopically. They *do* afford us, however, an inkling of the peak figures. More recent autopsy studies, several of which are included in Table I are of less value, since in most instances varying amounts of radiation had been employed before death, and this may have altered the picture. The figures based upon operative cases are of limited significance because there is no way of knowing just how completely the glands were removed, nor is it possible to know the finer shadings in the stages of advancement of the disease at the time of the operations. This is

readily understood when one recalls that in those days all cervical cancers were lumped into three great groups—operable, borderline, and inoperable. Even so-called operability has varied widely as the following figures testify:

Franz	81 %
Bonney	63 %
Wertheim	46 %
Stoeckel	70 %
Brunn	68 %
Zweifel	58 %
Ward	25.9%
Regaud	18.3%
Healy	24.5%
Lynch	30 %

These variations must have been due largely to individual differences in the interpretation of operability. Bonney estimated that he had operated upon 63 per cent of the patients presenting themselves to him for treatment. At the University of California, we have operated upon only 10 per cent of our cervical cancer cases although we have considered 30 per cent of the cases operable so far as the local extent of the growth was concerned. Obviously, Bonney has regarded as operable, many cases which we would have deemed too advanced for surgery. This wide variation in the clinical stage of advancement in cases operated upon, limits seriously the value of the figures quoted insofar as they pertain to a correlation with the extent of the local growth.

There have, however, been a few investigations in which attention has been focused more sharply on this point. Serial section studies of the tissues obtained at radical operations have been reported by Schauta, Baisch, Brunet, Oehlecker, Kundrat, Kermauner, and Sampson. All of these observers found an incidence of approximately 50 per cent glandular involvement in cases in which parametrial invasion was confirmed by microscopic examination. In cases in which the parametrium was microscopically free of cancer, Schauta found the glands involved in 2 cases out of 10; Oehlecker, in 31 per cent of 35 collected cases (Oehlecker 7, Schauta 10, Baisch 18); Kundrat, in 4 cases out of 36; and Sampson, in 3 out of 10 cases. In interpreting these figures, one should bear in mind that parametrial involvement or its absence as determined by the microscopic examination of serial sections does not always correspond with the palpatory findings on pelvic examination. The parametrium may be clinically free, yet actually contain cancer, or it may be indurated (by inflammatory reaction) yet contain no cancer. Since the determination of operability is inevitably linked with the palpatory findings, it becomes even more difficult to interpret the figures quoted. Other reliable findings which are less pertinent, but nevertheless interesting in this connection are as follows: Kundrat found involved glands in 32.5 per cent of 80

operative cases (serial sections); Kermauner, 43.8 per cent in 73 cases (serial sections); Brunet, 51 per cent in 47 cases (serial sections); Sampson, 47 per cent in 19 cases (serial sections); and Bonney, 40 per cent in 500 cases (*no* serial sections). Additional figures are given in Table I. One can conclude that parametrial involvement connotes glandular involvement in about one-half the cases, and uninvolved parametria indicate glandular metastases in one-third or less of the cases. Closer correlations cannot be derived from the literature.

The older studies have elucidated several interesting points, however. Winter, Baisch, Leveuf, Taussig, and others have shown that the so-called first stage glands comprising the obturator, hypogastric, ureteral, and sacral groups, were almost always involved first, while the second stage glands, such as the inguinal and lumbar groups, were involved usually only late in the disease, and, with the exception of 5 to 10 per cent of these cases, only after involvement of the first stage groups. These facts are of practical significance in that an attack upon the first stage glands, either operative or by radiation, might logically prove valuable, except late in the disease, or where there is palpable evidence of involvement of the second stage glands.

It has also been shown by many that gross enlargement of glands did not necessarily mean metastatic involvement. Conversely, unenlarged glands have been found involved by cancer. Finally, it has been observed that glandular metastases sometimes occurred even when the local cervical growth still remained clinically confined to the cervix, although the glands occasionally remained free even after considerable parametrial spread, a fact which must account for the cures which were obtained by surgery in cases with a rather extensive growth.

Selection of Cases

Taussig chose for his operations not the very early cases, because of the rather insignificant incidence of glandular involvement, nor the advanced cases, because of the improbability of curing the local growth, but the borderline cases (Stage II, *League of Nations Classification*). In this group, he felt that the chance of curing the local growth by radiation was relatively good, yet the rather high incidence of glandular spread often resulted in recurrence. In some cases he performed the operation before roentgen therapy and in others, immediately afterward. Our choice of cases has differed slightly in that we have selected for operation only those in which the immediate local reaction to radiation has been good, whereas, Taussig has performed his operations more routinely, and before he has had an opportunity to observe the character of the local reaction. Our feeling has been that it was useless to resect the regional glands if there was not a reasonable chance of a successful outcome so far as the cervix proper was

concerned. At that, we have often been mistaken, as death has not infrequently followed because of local recurrence. Our material is set forth in Table II.

TABLE II. PELVIC LYMPHADENECTOMY—65 CASES

	CASES WITH GLANDS INVOLVED	CASES WITH GLANDS FREE	TOTAL
A. Simple lymphadenectomy the object (Stage III Schmitz cases)			
Lymphadenectomy alone	6	19	25
Lymphadenectomy plus incidental hysterectomy	2	6	8
Failed*	2	0	2
Inspection only†	0	2	2
Totals for group	10	27	37
B. Hysterectomy the object but lymphadenectomy only performed			
Stage I	1	0	1
Stage II	1	3	4
Totals for group	2	3	5
C. Wertheim hysterectomy plus lymphadenectomy			
Stage I	0	5	5
Stage II	2	14	16
Stage V	1	1	2
Totals for group	3	20	23
Grand Totals (A, B, and C)	15	50	65

*In two, the glands were so extensively involved that removal was impossible. In one, cancer was later proved at autopsy. In the other, the patient died of obvious carcinomatosis though autopsy was not permitted.

†Twice the operation was discontinued after palpation revealed no enlarged glands. In all other cases the gland-bearing tissues were removed whether glands were palpable or not.

At the University of California, the Schmitz classification has been used so that it is not possible to make direct comparisons between our material and that of Taussig. As well as performing gland resections per se in our Stage III Schmitz cases in which the local cervical reaction to radiation was good, we have taken pains to resect the glands in earlier cases in which the Wertheim operation was being carried out. In a few instances when we have entered the abdomen for the express purpose of removing the glands having found the cervical region freely movable, we have performed the radical operation in addition. The average age of the 61 patients in whom the operations were completed was 41.8 years. The majority of the women were young as may be seen in the accompanying tabulation:

26 to 30 years	5 cases
31 to 35 years	10 cases
36 to 40 years	11 cases
41 to 45 years	17 cases
46 to 50 years	6 cases
51 to 55 years	6 cases
56 to 60 years	6 cases

In 35 cases, the patients received courses of high voltage x-radiation in addition to approximately 4,500 mg.hr. of radium distributed in and about the cervix before operation. The dose of roentgen therapy

varied between 2,000 and 4,000 r. to each of 4 fields, 2 anterior and 2 posterior. Both 1,000 kv. and 200 kv. machines were used. In 28 instances, radium only was used in small doses as preparation for the radical operation.

A.

B.

Fig. 1.—Degenerate cancer cells in regional lymph nodes. *A*, after vaginal radium only; *B*, after radium and x-radiation.

The operation which we have employed has been patterned after that developed by Taussig. It involves a laparotomy approach, the exposure of the depths of the broad ligaments and the lateral walls of the pelvis after removal of the tubes and ovaries, and resection of the gland bearing areolar tissues lying in the bifurcations of the common iliac arteries and in the obturator fossae. The areolar tissue about the uterine arteries and the ureters, as well as that lying about the iliac veins just before their exit beneath Poupart's ligaments have also been removed when glands could be palpated in these structures. The operations have not been difficult though occasionally they have been complicated by troublesome hemorrhage from the plexus of uterine veins. In two cases in which the Wertheim operation was performed in addition to lymphadenectomy, death from cellulitis and generalized pelvic infection followed within a period of two months; no cancer remained at autopsy. There has been no mortality from the operation of simple lymphadenectomy alone. In one case a broad ligament hematoma became infected and resulted in a prolonged illness from which the patient finally recovered. Obesity and old age have been considered contraindications.

Pathological Findings

If we omit the two cases in which the gland bearing tissues were palpated but not removed, lymph node metastases were found in 15 of the 63 cases. The figures relating to the incidence of glandular involvement (Table III) mean very little as such because of the small number and the heterogeneity of the cases, and because of the varying amounts of radiation employed. In many cases there were no grossly enlarged glands, yet invariably one or two and sometimes more glands were discovered in the areolar tissues from each of the hypogastric and obturator areas; these tissues were subjected to careful scrutiny in the laboratory. With two exceptions, the involved glands (15 cases) were grossly enlarged. There were many instances of enlarged glands which did not contain metastases. Several sections were cut from each recognizable gland, but no attempt was made to prepare serial sections. This is an obvious drawback to the study, and it must be admitted that serial sections might have revealed additional metastases. In the 13 cases in which metastases were found microscopically in glands, there was no question of their existence. These deposits

TABLE III. INCIDENCE OF GLANDULAR INVOLVEMENT

	CASES	CASES WITH GLANDS INVOLVED	PER CENT
Stage I	6	1	----
Stage II	20	3	15.0
Stage III	35	10	28.6
Stage V	2	1	----
Total	63*	15	23.8

*Omitting the 2 "Inspection only" cases.

were all squamous cell and all were similar to their parent tumors. In two cases (Fig. 1) some degree of degeneration appeared to be present. In one of these, the patient had received radium therapy preoperatively but no x-radiation (*A*), and in the other the patient had received 3,735 r. to left anterior and posterior fields (1,000 kv.) and 2,300 r. to right anterior and posterior fields (200 kv.), yet had this metastasis in the left obturator gland (*B*). In 11 cases there was no degeneration of consequence. (In only one of these 11 had the patient received roentgen therapy preoperatively.)

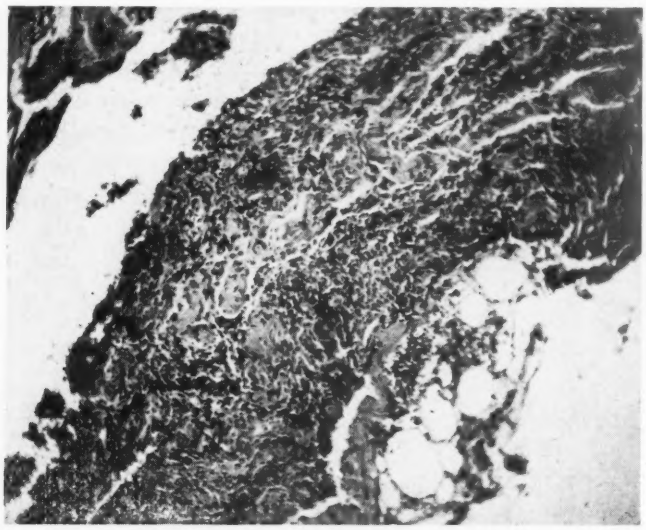

Fig. 2.—Fibrosis and hyalinization in a regional lymph node. This picture was observed both with and without preoperative x-radiation.

In other respects, it was difficult to distinguish the radiated (x-ray) from the nonradiated glands. In all instances, there were varying degrees of endothelial and follicular hyperplasia. Fibrosis and hyalinization were common but were not distinctive, having been observed in 24 of the 33 cases in which preoperative x-radiation had been employed, but also in 10 of the 28 cases in which the patients had received no roentgen therapy. (Fig. 2.) No correlation with the amount of x-radiation could be established. A point of interest was the finding of glandular inclusions in the glands from two cases. These we interpreted as benign. Such a finding has been the bone of much contention in France. Schauta, Brunet, Gricouroff, and others have reported similar findings and interpreted these structures as endometrial glands. Wertheim found lymph nodes containing glandular inclusions 48 times in 500 operative cases. Basing his belief upon the subsequent course of these patients, he regarded such inclusions as benign. Michel-Bechet and Taussig have made similar observations. These authors favor the idea that the condition is one of endometriosis.

Of great interest are the figures on the incidence of glandular involvement when the cases are broken down into those in which the patients received preoperative deep x-ray therapy, and those in which they did not. (Table IV.) Obviously, the figures are too small to regard as true reflections of the percentages of glandular involvement to be expected in patients treated with and without radiation. However, the 39.3 per cent glandular involvement following *no* preopera-

TABLE IV. INCIDENCE OF GLANDULAR INVOLVEMENT IN RELATION TO PREVIOUS ROENTGEN THERAPY

	STAGE	CASES	GLANDS NORMAL	GLANDS INVOLVED	PER CENT
No preoperative roentgen therapy	I	6	5	1	
	II	16	12	4	
	III	5	0	5	
	V	1	0	1	
	Total	28	17	11	39.3
Preoperative roentgen therapy	II	4	4	0	
	III	30	26	4*	
	V	1	1	0	
	Total	35	31	4	11.4

*Includes the 2 cases in which involvement of the glands was so extensive that removal was impossible.

tive x-radiation would seem to be quite significant when compared with the 11.4 per cent glandular involvement in cases in which roentgen radiation was used, particularly when we consider that the latter group contained many more advanced cases than the former. If this highly suggestive difference in the incidence of glandular involvement in the two groups of cases can be substantiated by future experience, one would like to interpret it as evidence that high-voltage roentgen therapy is capable of destroying, and often does destroy cancer in the regional nodes. In Taussig's last report, the incidence of glandular metastasis was given as 26.8 per cent which was lower than that shown in previous reports (33 per cent in 1936). He remarked, "Apparently, this was due to the prolonged and heavy x-radiation patients have received preoperatively in recent years." However, he believed that cancer metastases might frequently be rendered unrecognizable (by radiation) but not wholly destroyed, and thus that the operative removal was still justifiable.

Results

The actual five-year results in this group of cases are of little significance in evaluating this procedure as a method of treatment. (Table V.) It is of interest that the lives of at least three women from whom glands involved by cancer were removed, were apparently saved by the procedure. Of the 10 patients in the five-year group in whom the glands were involved, only three survived, while of 18 patients in whom glandular involvement was not found, 16 survived the five-year period. While these figures seem to point a very ominous finger at

TABLE V. RESULTS

Total five-year cases	28
Alive and well after five years	19
Number in which involved glands were found	3
Number in which no involved glands were found	16
Died in less than five years	9
Number in which involved glands were found	7
Number in which no involved glands were found	2

glandular involvement, at least 5 of the 9 deaths were due to the local cervical recurrence and invasion of cancer, and not to the existence of cancer in the glands.

Discussion

If the premise upon which Taussig based his operation, namely, that metastases in lymph nodes are peculiarly resistant to radiation, can be substantiated, then his procedure deserves a much more extended trial. If however, it can be shown that modern x-radiation may actually destroy metastatic cancer in lymph nodes, then this nonoperative and possibly more comprehensive method may prove superior. The number of cases so far subjected to the procedure of lymphadenectomy is insufficient to determine definitely its sphere of usefulness in the treatment of cervical cancer. The distinctly lower incidence of glandular involvement in our series when the operation was carried out after x-radiation suggests that modern roentgen techniques may make lymphadenectomy unnecessary. Certainly the results call for an extension of experience in cases subjected to preoperative x-radiation as compared with those in which no preoperative x-radiation has been employed as this appears to be the crux of the whole matter.

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Discussion

DR. WILLIAM P. HEALY, New York City.—During the past 25 or 30 years, radiation therapy has largely supplanted surgical procedures as the method of choice in the treatment of cancer of the cervix.

About 1930, Taussig was impressed by the large number of Group II (*League of Nations Classification*) cases of cancer of the cervix in which the primary disease was cured by radiation therapy, but the patients died of metastatic cancer. He assumed these deaths were largely due to the failure of the methods of radiation therapy then available to cure the cancer which already had involved the pelvic lymph nodes. It was in this relatively favorable group that it seemed to him possible to obtain more five-year cures by combining iliac or pelvic lymphadenectomy with radiation therapy.

In 1943, Taussig reported 175 lymphadenectomy operations done by him and his associates and he stated that the low primary mortality, about 1.5 per cent, and the relatively high survival rate in their five-year cases convinced him that this combination of surgery with thorough radiation in Group II cases of cancer of the cervix was of definite value. Many of us were favorably impressed by Taussig's views, but failed to follow the procedure except sporadically.

Dr. Morton's paper in which he reports 65 cases of pelvic lymphadenectomy is a valuable contribution to the subject. I am inclined to believe from his report that roentgen therapy was much more adequately administered in his cases than in Taussig's. This, of course, would be accounted for by improved technique and higher voltages in recent years. One must be impressed by the distinctly lower incidence of pelvic lymph node involvement in Morton's series when adequate roentgen radiation had preceded the operation. As he says, it would suggest that improvement in modern x-ray technique may make the operation of lymphadenectomy unnecessary.

In 1942, Healy and Twombly reported a study of 920 cases of primary cancer of the cervix treated at Memorial Hospital from 1932 to 1937. These cases were studied from the viewpoint of "The Effect on the Rate of Cure of Increased Roentgen Radiation to the Parametria." It was found that the more modern divided dose technique of roentgen therapy which requires about three weeks of daily treatments to accomplish definitely raised the five-year cure rate in all cases. Nevertheless, the best five-year cure rate that we were able to show in our Stage II cases was 50 per cent. Therefore, it would seem to me desirable, in fact an obligation, for us to add pelvic lymphadenectomy or some other surgical procedure to the combined radium and roentgen therapy in a selected list of our Group II cases of cancer of the cervix.

It seems to me that gynecologists are about to enter on a new era in the treatment of cancer of the cervix which has become feasible because of improved methods of anesthesia, better preparation for operation and better postoperative care because of the use of intravenous fluids, blood serum and whole blood, and lastly in the protective use of sulfa drugs and penicillin. It is my impression that we will henceforth carry out more extensive surgical procedures combined with radiation

therapy than has been done in the past 25 years, in properly chosen cases. I think the surgeon who fails to qualify for this will miss an opportunity, for in the final analysis surgery has always been the best approach to the treatment of cancer, and radiation, while useful and curative in certain cases, is not the final answer.

DR. LEWIS C. SCHEFFEY, PHILADELPHIA, PA.—Dr. Morton believes his operation indicated in those patients in whom regional node metastasis may exist through the primary cervical growth seems to have responded sufficiently well to irradiation. He recognizes, however, that while an apparently early lesion may already have spread to the regional nodes, one more advanced in appearance may be relatively localized, even with parametrial involvement.

I am particularly impressed with the high incidence of younger women in the series presented, 43 per cent, and wonder as a matter of interest how this selected figure compares with the general incidence of cervical carcinoma in women 40 years of age or younger in the University of California Clinic. At Jefferson Medical College Hospital 27 per cent of the cervix cancers occurred in women before the menopause.

All in all, Dr. Morton found lymph node involvement in 15 or 23 per cent of the 65 cases observed, but he is careful to state that one cannot exclude the possible effect of preoperative irradiation upon this finding. Of more importance, I think, is the breakdown of this figure which shows a decided advantage in favor of thoroughly employed preliminary irradiation therapy. These observations seem to demonstrate the potent effect of adequate irradiation on the regional nodes not only when the possibility of subsequent surgery is entertained, but in all advanced cases as well. That degeneration did occur in some of the lymph nodes is surely significant. Naturally, these findings must be substantiated by further work if we are to decide to rely solely upon irradiation therapy, or if we are to complement it by pelvic lymphadenectomy, or in some cases by radical hysterectomy.

Surgery has played no part in the treatment of cervical carcinoma in the Jefferson Clinic since 1923, two years after its establishment. The Group 1 and 2 patients (Schmitz classification) that we have encountered have amounted to but 12 per cent among nearly 500 patients seen, and that is one reason why we have depended upon irradiation therapy in practically all cases. Another reason has been the relatively satisfactory results seen with this therapy to date. Our most recently reported statistics show a five-year survival rate of 75 per cent in Group 1 patients, and 43 per cent in Group 2 patients, or a combined rate of 47 per cent in the so-called "early" cases. In view of what Dr. Morton has shown us today, together with the results of Dr. Taussig's earlier efforts, I shall feel derelict if we do not attempt work of a similar nature, even in Group 3 patients who have responded well locally to irradiation therapy.

DR. JOE V. MEIGS, BOSTON, MASS.—I have been immensely impressed by the work of Dr. Taussig, whose operating I observed in 1940. Dr. Lynch in California was very much interested at that time as to whether we should carry out Dr. Taussig's ideas or do radical hysterectomies.

I am now doing the Wertheim operation on those patients who are good surgical risks. We had felt before beginning work with this procedure that our mortality would be excessive. We have, however, now done about 65 Wertheim operations, that is, removing all the pelvic lymph nodes and taking out as much parametrium and as much vagina as possible, and there has been no mortality. Our low mortality is due to modern surgery and modern methods of taking care of the patient both before and after operation.

My objection to the Taussig operation is that the lymph node area about the cervix is not properly taken care of. Unless one removes this area, one cannot get all of the lymph nodes, although Dr. Taussig with whom I discussed this matter felt that radiation handles that particular area. We have found that 15 per cent of

our cases had positive lymph nodes. Cancer in a radiated cervix may recur after ten years and radium cannot destroy cancer in lymph nodes. It is my distinct impression that the Taussig operation is not sufficient and that it must have added to it the removal of the uterus and the parametrium. It is a formidable procedure, but in our hands at the present time, it is so successful that we feel we have a right to proceed further.

DR. MORTON (closing).—The average age of the patients operated upon is considerably less than that for our series in general. We selected the younger women for this operation because we felt that many of the older ones were not good operative risks.

Our usual routine is to give x-ray therapy first and the radium treatment later, particularly when the growth is bulky. The idea behind this routine is that a good deal of shrinkage and a good deal of cleaning up of the infection will result so that the radium can be applied more safely and effectively at a later time. However, we have reversed this order in certain cases, more particularly in those in which the growth was earlier or small in area. We have also reversed the order in older women where we felt we might not be able to carry through the x-ray therapy because of its drastic general effects. We feel that our results have justified the initial use of radium and the frequent omission of x-ray therapy in these types of cases. I am very much interested that Dr. Meigs has taken up the complete operation, and his reactions to it. As most of you know, Dr. Lynch, from whose service this series of cases was taken, has been much interested in the radical operation for a great many years, and yet the operation has been performed on not more than one-tenth of all the patients seen on his service. This seems to point to a very limited, though definite field of usefulness. While 30 per cent of our cases have been considered operable from the point of view of the local extent of the growth, in two-thirds of this operable group the radical operation was considered to be contraindicated by virtue of old age, obesity, or the like.

PREGNANCY AND OTOSCLEROSIS*

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(From the Department of Obstetrics and Gynecology, University of Illinois)

OTOSCLEROSIS is a chronic, nonsuppurative disease of the bony capsule of the ear surrounding the labyrinth which interferes with the function of hearing. This disease is characterized by progressive absorption of the normal capsular bone and replacement with new spongy bone. This bony change often leads eventually to stapedio-vestibular fixation and complete deafness. The site of predeliction is above and in front of the oval window.[1] (Fig. 1.)

Otosclerosis or, as the French call it, otospongiosis, is found predominately in females, 66 to 79 per cent. Shambaugh[2] has estimated that 45 per cent of adult deafness is due to this disease. Fowler[3] has suggested, and subsequent observations have substantiated his thesis, that routine histological examination of temporal bones will often reveal an existing focus which does not involve the footplate, and therefore, does not produce deafness. These facts then would suggest that otosclerosis is rather a common disease. Nash,[4] on the other hand, states that no diagnosis of otosclerosis can scientifically be made without progressive deafness, Bezold's triangle, and a normal middle ear and eustachian tube. This author was able to make a definite diagnosis of otosclerosis in less than 6 per cent of 1,000 cases of deafness which he studied.

Politzer (over 50 years ago) first described otosclerosis, and since that time, it has been the subject of intensive study. Little knowledge, however, has been added during this period concerning its etiology. Early in these investigations the great importance of heredity was recognized and numerous families have been followed carefully. An interesting study covering 5 generations is reported by Ulrich[5] as follows:

In the first half of the eighteenth century, a married couple in Zurich with perfectly normal hearing had 3 daughters congenitally deaf. Marriage of one daughter to a young man of normal hearing was forbidden but later consummated. This pair had several normal children but also 3 daughters congenitally deaf. Thus in 2 successive generations 6 deaf children were born, with only one deaf parent. Actually all had originated from a pair of normal-hearing persons. Three hundred and ninety decendants of this family were traced, but no further cases of deafness could be ascertained.

The first study of otosclerosis in identical twins was reported by Albrecht[6] in 1932. Since this time several additional cases have been

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observed by Rodin[7] in 1933, Shambaugh and Shambaugh, Jr.,[8] in 1933, and Shambaugh,[9] Jr., in 1935. In 1941, Hagens[10] recorded the family history of a set of identical twins with their audiometric tracings. The mother of these twins came from a family of 10 children, 8 of whom were deaf. An increase in deafness occurred in the mother shortly after the birth of the twins. A similar decrease in sound perception occurred in one of the twins after the birth of her baby. These changes, however, are not substantiated by audiometer readings. The hearing defect in the second twin was not severe enough to cause her to seek medical aid. On examination however, it was found to be bilateral, and tests permitted a diagnosis of otosclerosis. More recently Fowler[11] records the case histories of 3 sets of deaf identical twin girls. In only one of these was there any impressive familial history of deafness, a grandmother and a maternal aunt. The mother herself had perfect hearing. No effect of menstruation or childbearing on hearing could be determined in these twins except one girl had more difficulty in hearing when she was nervous at menstruation.

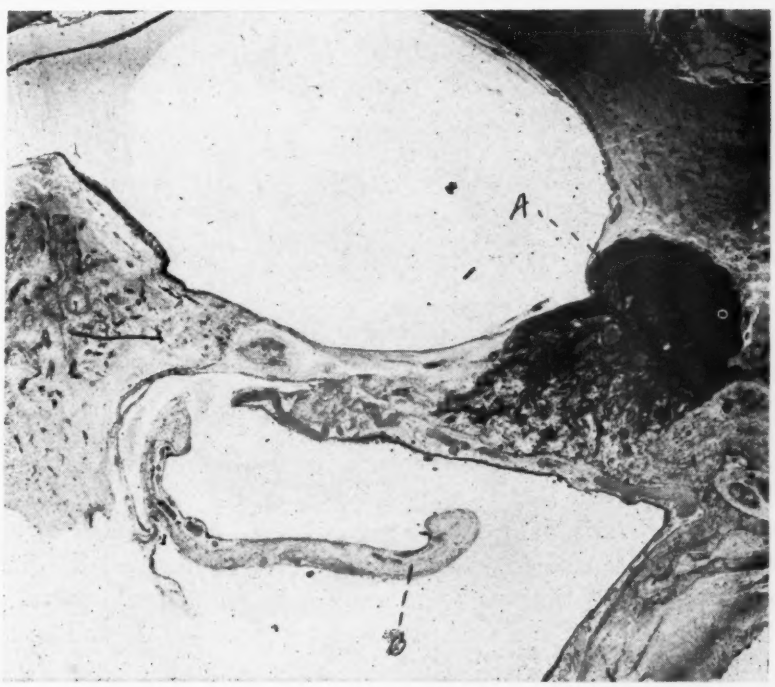


Fig. 1.—Showing area of otosclerosis. *A*, in region of oval window; *B*, stapes.

Guggenheim[12] in his monograph concludes that otosclerosis is primarily an hereditary disease. In this splendid work the author reports a careful study of a 6-week-old, perfectly preserved fetus from a classic case of otosclerosis. Rather typical histologic findings were present in the capsular bone of the ear. He makes a plea to those of us

engaged in obstetrics for help in the further collection of similar valuable material. Fetuses, in any stage of their development, born of mothers suffering from deafness which become available to any of us for post-mortem examination should be carefully studied by a competent otological pathologist. Our group could profitably join with the otologists in a study of this condition during pregnancy.

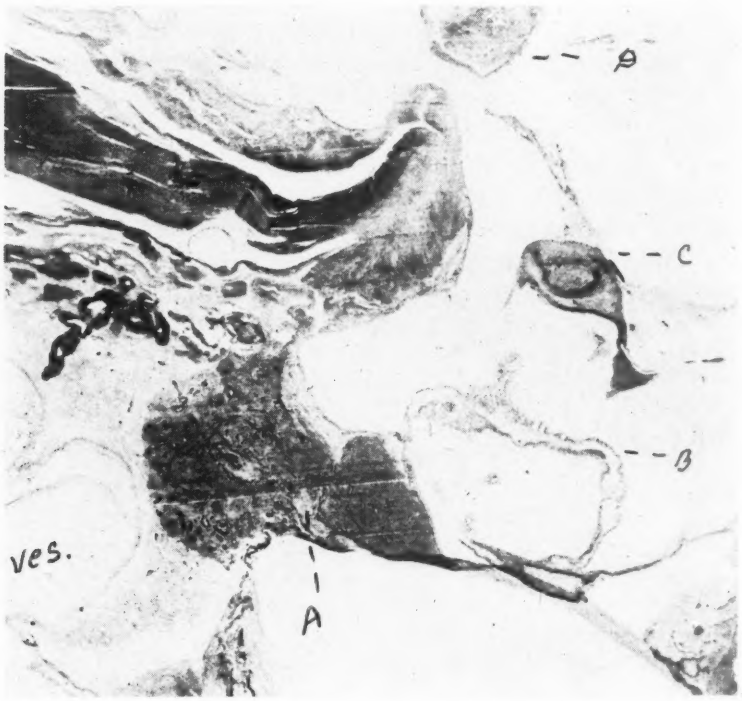
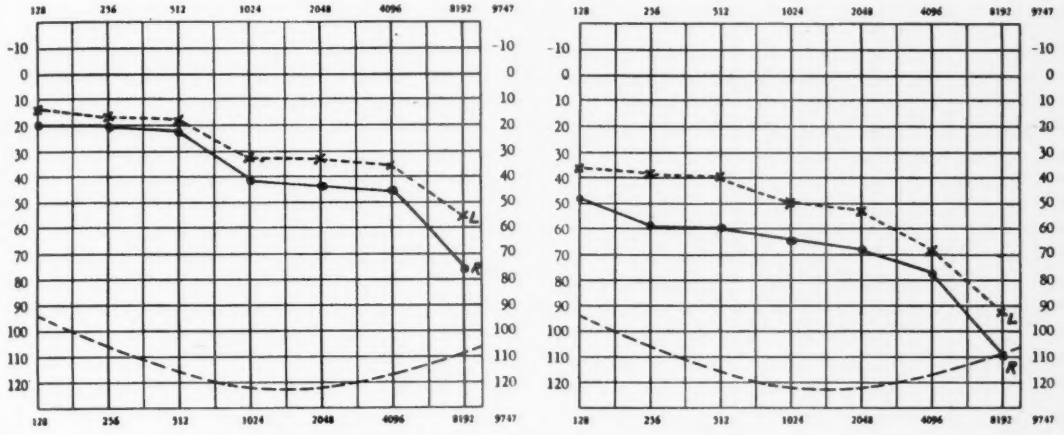


Fig. 2.—Showing area of otosclerosis. *A*, stapes; *B*, incus; *C*, malleus, *D*, vestibule (Ves).

Most American standard textbooks of obstetrics do not mention otosclerosis.[13-15] or they list it among the indications for therapeutic abortion.[16, 17] Adair and Steiglitz[18] state that there is a familial tendency to otosclerosis in approximately 50 per cent of cases but that pregnancy is almost negligible as an etiological factor. Adair[19] believes that deafness and tinnitus are increased in only about one-third of cases. He feels that the condition does not threaten life and is, therefore, not an indication for prevention or interruption of pregnancy. We can corroborate his statement that the desire for pregnancy will often outweigh the possibility of further impairment in hearing and is rarely an indication for the interruption of pregnancy. Personal observation of several cases of pregnancy complicated by this form of deafness plus the desire to advise adequately a sterility patient suffering from otosclerosis led us to this present study. The conclusions are based on the available literature, personal observation of 5 afflicted patients, and a

compilation of as many case records as we were able to collect from the many kind friends who have allowed us to use their records. (Total 72.)

A review of the literature suggests several important but confusing angles to the present concept of the importance of marriage, pregnancy, abortion, sterilization, castration or nursing on the transmission of otosclerosis. Widespread interest in these questions was first aroused by many reports occurring in the German literature, although the first laws dealing with the subject were enacted in a small liberal Swiss canton.[5] Shambaugh,[20] following a review of the literature in 1938, says, "The German law for the prevention of the propagation of hereditary disease is responsible for the continued interest in hereditary deafness in the German literature." One is forcibly struck by the obvious effect of the idea for the betterment of the race on the therapeutic



Pt. C, July 1935, Before pregnancy

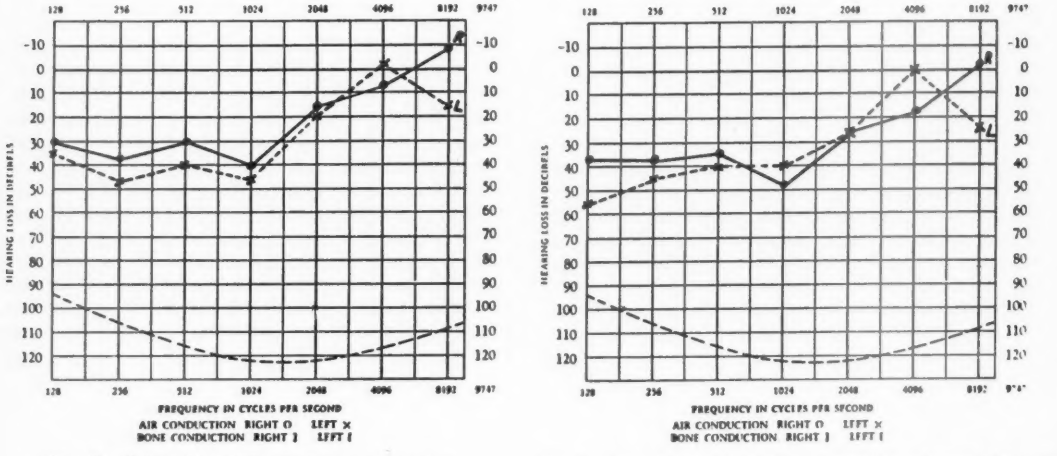
Pt. C, May 5,1939, After pregnancy

Fig. 3.

measures advised and the conclusions drawn by Teutonic authors. Analysis of a problem on the basis of political ideology does not lend itself to scientific accuracy. In a similar manner, religious precepts have apparently influenced many of the French otologists in arriving at conclusions directly opposed to those of their German confreres.[21] As yet, no unbiased agency has had sufficient personal or collected experience to speak authoritatively on the subject.

While most authorities are agreed as to the great importance of heredity, many of them have suggested other possible etiological or contributory factors in otosclerosis. Fowler[22] has expressed the belief that head colds and the development of the condition are related. Selfridge[23] suspected a faulty diet, especially one low in citrus fruits, milk and eggs. Many otosclerotics have poor crumbling teeth without much evidence of infection. The identical twins, previously mentioned, were both wearing upper plates at nineteen years of age.

Bunch[24] has observed a similar dental difficulty especially in those patients with low metabolic rates. Davenport[25] concludes that otosclerosis represents genetically two dominant factors, one sex linked. Symptoms of otosclerosis are usually manifested at puberty or later. An increase in the deafness often occurs at the time of the menopause.[26] Most authorities are agreed that the disease is at least temporarily adversely affected by pregnancy and lactation. However, Guggenheim says there is no scientifically proved glandular etiological factor in this disease. Fowler could find no abnormality of general metabolism in a large number of patients thus affected. Weber[27] is quite sure that the local form of osteodystrophia fibrosa is due to some local disturbance in metabolism. Despons has found that consanguineous marriages frequently result in this condition. Gottlieb[28] doubts the validity of genetic studies on the heredity of deafness and suggests persisting environmental factors leading to nutritional and toxic disorders as a possible cause.



Pt. B, July 24, 1936, Before pregnancy

Pt. B, September 30, 1937, 3 months after delivery.

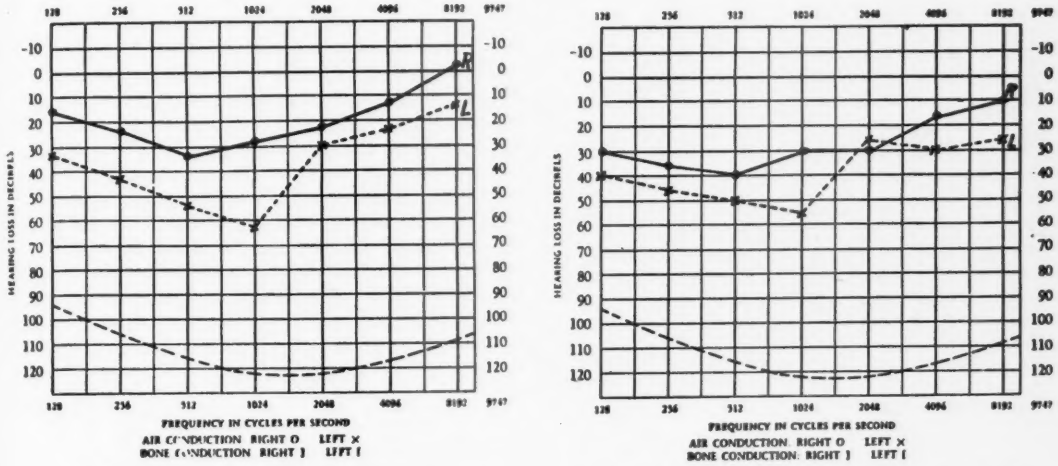
Fig. 4.

Falta,[26] in a study of 76 women in whom otosclerosis appeared after the fortieth year, noticed that 11 developed the difficulty with hearing during the climacterium. Furthermore, 8 of these 11 women had borne several children without any apparent impairment of hearing.

Despons says that total sterilization or an oophorectomy are sometimes held responsible for, or predispose to, the advance in deafness. Escat[21] had a case in which hysterectomy was followed by deafness. Schmidt,[29] in a study of 106 cases of otosclerosis, says the deafness increased under various conditions, i.e., trauma, prolonged anxiety or excitement, menstruation, appendicitis and many other illnesses.

Despons in summarizing a symposium on the subject of otosclerosis and pregnancy says, "In a few years (otosclerosis) will probably be

listed among social evils and eugenics may require prophylaxis. Recently, the tendency has been to favor abortion in otosclerosis, not so evidently in France as across the Rhine." Despons goes on to quote Goerke. "Abortion is not indicated in pregnancy with otosclerosis if the deafness is minimal. If preceding pregnancies have increased it and there exist ear noises and psychic depression, removal of the ovaries or sterilization by x-rays should be advised to prevent further increases in deafness."[30]


HEARING LOSS IN DECIBELS
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AIR CONDUCTION RIGHT O LEFT X
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HEARING LOSS IN DECIBELS
FREQUENCY IN CYCLES PER SECOND
AIR CONDUCTION RIGHT O LEFT X
BONE CONDUCTION RIGHT] LEFT [

Pt. A, August 31, 1925, Before marriage

Pt. A, January 6, 1928, 4 months pregnant

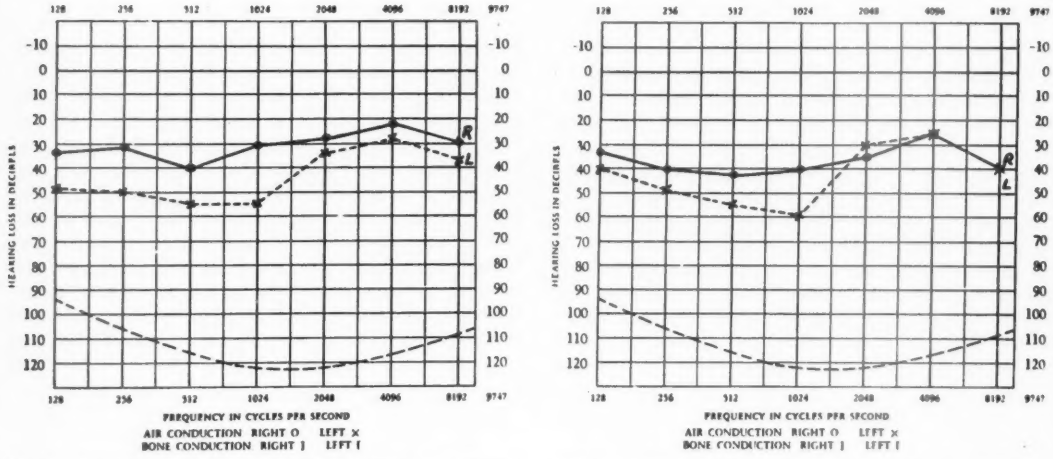
Fig. 5.

Mortimer and his co-workers[31] have shown the marked changes which occur in the mucous membranes of the respiratory tract during pregnancy. These investigations have also produced a similar change of the respiratory passages in the *Macaca* monkey by the administration of estrogenic hormones. A definite perivascular edema in the submucosa and changes in the connective tissue occurred which are very similar to those found in the sex skin about the genitals.

It seems reasonable to believe that the high estrin levels which occur during pregnancy in the human female may exert a similar effect on the mechanism of hearing. Otological complaints during pregnancy are very common, but most of them tend to disappear when involution has occurred. These facts may almost entirely account for the frequent appearance of otosclerosis for the first time during the primiparous pregnancy. In fact these changes may adequately explain a large proportion of the loss of hearing during the course of reproduction. Further clinical and experimental observations concerning the effect of pregnancy on the respiratory and auditory systems in the human female are essential for the further consideration of these problems.

Greifenstein,[32] studying 98 women with otosclerosis in a group of 122 patients with difficulties in hearing who had been reported to the state

for therapeutic abortion and sterilization, attempted to explain the obvious variations in indications and results in the then current methods for the estimation of hearing. These difficulties arose because at that time there was no exact definition of what constituted "worse hearing."



Pt. A, August 28, 1928, 2 months after delivery

Pt. A, July 8, 1932, after second pregnancy

Fig. 6.

Now, with the audiometer, we have a more exact method of measuring loss or gain in hearing.[33] This can be measured in decibels and the differences of sound perception in various tonal areas can be determined. (Figs. 3-6.)

If the metabolic concept of the etiology and progress of otosclerosis is tenable, recent improvement in prenatal care may account for at least some of the less pronounced losses of hearing during pregnancy shown

TABLE I. STATISTICS

Cases with audiograms		
Personal communication	13	
From the literature	5	
Total		18
Cases without audiograms		
Personal communication	19	
From the literature	35	
Total		54
Number of patients in whom hearing remained the same or otologist felt decrease in hearing was that which might be expected during the normal progress of the disease		
Cases without audiograms	24	
Cases with audiograms	8	
Number of patients in whom hearing was decreased beyond normal expectancy		
Cases without audiograms	30	
Cases with audiograms	5	
Number of cases in which deafness first occurred during pregnancy		14

TABLE II. CASES WITHOUT AUDIOGRAMS (BY PERSONAL COMMUNICATION)

CASE	AGE	RECORD OF DEAFNESS IN FAMILY	OBSTETRIC HISTORY	EFFECT OF PREGNANCY ON DEAFNESS	
M. R.	39	0	Para 1	Pregnancy did not influence hearing	Goldberger, M. A.
H. Z.	32	Deafness in family	Para 2	Pregnancies did not influence hearing	
P. K.	34	0	Para 2	Slight increase in deafness	
L. B.	-	0	Para 2	Slight deafness during second pregnancy	
W. M. C.	39	0	Para 4	Deafness appeared during second pregnancy. Improvement after delivery	Cody, C. C.
H. W.	41	0	Para 1	Pregnancy did not influence hearing	Dieckmann, W. J.
D. M.	28	0	Para 1	Pregnancy did not influence hearing	
A. B.	37	Mother, brother	Para 3	Pregnancy did not influence hearing	Johnston, R.
F. C. R.	35	0	Para 1	Pregnancy did not influence hearing	Galloway, C. E.
E. M. K.	41	0	Para 1	Pregnancy did not influence hearing	
R. G. B.	27	0	Para 1	Pregnancy did not influence hearing	
R. D.	46	0	Para 2	Deafness developed during first pregnancy	
J. S.	-	Paternal and maternal grandparents, father, brother	Para 3	Pregnancy did not influence hearing	Johnston, R.
T. C.	-	Mother, sister (twin)	Para 3	Deafness appeared during first pregnancy, increased during second and third	Gough, J.
R. H.	40	0	Para 2	Deafness increased after pregnancies	
E. M. A.	34	Father	Para 3	Deafness appeared during first pregnancy, increased after second and third	Shambaugh, G. E., Jr.
M. K.	47	0	Para 11	Deafness appeared during last 3 months of eighth pregnancy. Three subsequent pregnancies	Shambaugh, G. E., Jr.
D. F.	39	0	Para 2	Otosclerosis? Hearing tests showed nerve deafness. Deafness progressive, with increase after both pregnancies	Shambaugh, G. E., Jr.
B.	32	Paternal grandfather	Para 2	No appreciable change in hearing except natural progression indicated by biannual audiograms	Biehn, J. F.

TABLE III. CASES WITHOUT AUDIOGRAMS (FROM THE LITERATURE)

CASE	AGE	RECORD OF DEAFNESS IN FAMILY	OBSTETRIC HISTORY	EFFECT OF PREGNANCY ON DEAFNESS
2[1]	30	0	Para 1, age 22	Deafness appeared during pregnancy
4	33	Father, sister	Para 1, age 27	Deafness appeared during pregnancy
6	66	0	Para ?	Pregnancy did not influence hearing
7	26	Maternal grandmother	Para?	Deafness appeared during pregnancy
9	37	0	Para ?	Pregnancy did not influence hearing
12	52	Maternal grandfather	Para ?	Pregnancy did not influence hearing
14	31	Mother	Para 3	Hearing worse after pregnancies
15	28	Mother	Para 1	Deafness appeared after pregnancy
16	31	0	Para 2	Deafness appeared after second pregnancy
18	38	0	Para 2	Deafnes increased after both pregnancies
20	26	Mother	Para 2	Deafness increased after both pregnancies
21	54	0	Para ?	Pregnancy did not influence hearing
22	41	0	Para 2	Pregnancy did not influence hearing
23	35	Father	Para 2	Pregnancy did not influence hearing
29	24	Uncle, aunt	Para 1	Pregnancy did not influence hearing
34	29	0	Para 4	Deafness increased after first pregnancy
35	38	0	Para 1	Deafness increased during pregnancy
36	33	Mother	Para 2	Pregnancy did not influence hearing
37	24	0	Para 2	Deafness increased after both pregnancies
4-B-4[2]	?	Brother, sister	Para 3	Pregnancy did not influence hearing
1-C-4		Father, brother, grandfather, 2 uncles, cousin	Para 10	Deafness increased after pregnancies
1-2-C-1		Mother, 2 sisters, grandfather, 3 aunts	Para 4	Deafness increased after pregnancies
1-B-4		Father, 2 sisters	Para 9	Deafness increased after pregnancies
1-2-C-5		Mother, 2 sisters, grandfather, 3 aunts	Para 2	Deafness noticed after pregnancies
1-2-C-8		2 sisters, 2 uncles, aunt, grandfather	Para 4	Deafness increased after pregnancies

[1]Bunch, C. C.: Ann. Otol., Rhin. & Laryng. 43: 344, 1934.
[2]Schick, H. F.; Goldstein, M. A.: Laryngoscope 46: 731, 1936.

TABLE III—CONT'D

CASE	AGE	RECORD OF DEAFNESS IN FAMILY	OBSTETRIC HISTORY	EFFECT OF PREGNANCY ON DEAFNESS
Case 4[3]	46	0	Para 4	Deafness occurred with first pregnancy. Increased after the other three
Case 9	34	Mother, maternal grandmother, 2 cousins	Para 1	Deafness occurred with first pregnancy
Case 18	27	Paternal aunt	Para 1	Deafness increased after pregnancy
Case 21	29	Mother	Para 1	Deafness occurred with first pregnancy
2-5[4]	50	0	Para 7	Deafness increased after pregnancies
3-14	62	Mother	Para 3	Pregnancy did not influence hearing
L. B.[5]	32	0	Para 2	Pregnancy did not influence hearing
Case 1[6]	30	0	Para 2	Deafness increased after first pregnancy. Hearing markedly improved in seventh month of second pregnancy. Deafness much worse after second delivery
Case 2	45		Para 3	Deafness decreased during last month of first and second pregnancies. Improvement disappeared after confinement. No change during third pregnancy
A. S.[7]	22	-	Para 3	It is difficult in any way to see that pregnancy influenced hearing

[3]Lempert, J.: Arch. Otolaryng. 28: 42, 1938.
[4]Davenport, C. B.; Milles, B. L.; Frink, L. B.: Arch. Otolaryng. 17: 340, 1933.
[5]Fowler, E. P.: Laryngoscope 52: 725, 1942.
[6]Ashcroft, D. W.: J. Laryng. & Otol. 50: 268, 1935.
[7]Bunch, C. C.: Laryngoscope 49: 805, 1939.

in the following case reports. Better nutrition, high vitamin and mineral supplements to the diet, prompt cure of a respiratory disease and correction of metabolic defects can surely be of service to the otosclerotic patient.[34-37]

Timely education in lip reading and the employment of the improved type of hearing aids will do much to soften the impact of the more apparent degrees of deafness.[38] Safe operative cure of this condition awaits further developments along the lines of the present fenestration operation.[39-41]

Conclusions

1. Our attempts to collect these data have convinced us that difficulties in hearing during pregnancy are frequently overlooked, neglected entirely, and often inadequately studied.

2. A very careful family history concerning deafness should be taken on every pregnant woman who experiences appreciable changes in hearing.

TABLE IV. CASES WITH AUDIOGRAMS (BY PERSONAL COMMUNICATION)

CASE	AGE, DATE	FAMILY HISTORY OF DEAFNESS	AGE AT ONSET OF DEAFNESS	OBSTETRIC HISTORY	AUDIOGRAMS			COMMENT
					BEFORE	DURING	AFTER	
H. M B.	32	-	23	Para 1 July, 1937 Para 2	Between Sept., 1935, and Sept., 1937, there was a loss of 7 decibels in the right, and no loss in the left			"Loss of hearing normal for this length of time." Shambaugh, G.
McC.	-	-	-	Para 1 Para 2 Two pregnancies between audiograms	Jan., 1934 R 18-25 L 36-55		June, 1938 R 22-30 L 38-60	Hayden, D. B.
D.	-	-	-	Para 1	Jan., 1938 R 19-27 L 34-50		Feb., 1939 R 17-28 L 33-60	Hayden, D. B.
S.	-	-	-	Para 1	April, 1938 R 30-48 L 21-40		March, 1939 R 46-69 L 33-63	Hayden, D. B.
H. J.	-	-	-	Para 1	July, 1935 R 15-70 L 20-90		May, 1939 R 36-90 L 50-95	Hayden, D. B.
W.	-	-	-	Para 1 Oct., 1937 Para 2 Aug., 1942	Oct., 1939 R 50-50 L 40-55	Feb., 1942 R 35-55 L 10-30	March, 1944 R 30-55 L 30-50	Hayden, D. B.
B.	-	-	-	Para 2 May, 1942	June, 1941 R 25-50 L 30-55		April, 1943 R 20-60 L 20-60	Hayden, D. B.
L. N.G.	-	-	-	Para 1	Audiograms same before and after pregnancy			Fowler

W. W.	33 in 1942	-	22	Para 1 Sept., 1932 Para 2 Miscarriage Para 3 Oct., 1934	Jan., 1931 R 20-40 L 46-56 June, 1933 R 31-43 L 31-56		Oct., 1932 R 24-50 L 30-58 Dec., 1934 R 34-54 L 44-58 Sept., 1936 R 50-56 L 50-60 Dec., 1939 R 40-70 L 40-70	60% cases of otosclerosis affected by pregnancy Advises therapeutic abortion at fourth or fifth month Tobey, G. L., Jr. Irving, F. C.
G. R. H.	-	0	-	Para 1	R 40-56 L 15-35		R 53-73 L 45-60 (5 months post partum)	Tobey, G. L., Jr.
L. T. H.	-	0	-	Para 1 June, 1928 Para 2 March, 1932	Aug., 1925 R N-33 L 13-65 Oct., 1930 R 40-50 L 40-55	Nov., 1927 R 10-45 L 25-65 Jan., 1928 R 10-40 L 25-55 Dec., 1931 R 20-45 L 25-55	Aug., 1928 R 30-40 L 36-55 July, 1932 R 25-41 L 36-55 March, 1940 R 22-42 L 30-55	Tobey, G. L., Jr.
H. S. A.	34	Father	1932 (24 yr.)	Para 1 Jan., 1930 Para 2 May, 1932 Para 3 Nov., 1934	 Oct., 1931 R 20		 Feb., 1937 R 40	"Deafness noticed during second pregnancy. Increased during third. Therapeutic abortion Nov., 1934. Hearing improved." Friedberg, S.
R. S.	30	Father	1 yr.	Para 1	R N L 40-48	R 0-10 L 42-48		"No appreciable change in hearing during pregnancy." Friedberg, S.
F. A.	22	0	4 months? 2 years	Para 1	R N L 20-50	R N L 20-40 (3 mo. pregnant)	R N L 15-50	"Hearing improved 10 decibels at 3 months." Friedberg, S. Curry, L. T.

TABLE V. CASES WITH AUDIOGRAMS (FROM THE LITERATURE)

CASE	AGE AND DATE	FAMILY HISTORY OF DEAFNESS	AGE ONSET OF DEAFNESS	OBSTETRIC HISTORY	AUDIOGRAMS BEFORE	AUDIOGRAMS DURING	AUDIOGRAMS AFTER	COMMENT
M. S.	27 in 1937	0		Para 1 June 5, 1937	May 8 R 35-75 L 45-85		June 9 R 40-85 L 35-55 Dec. 21, 1938 D 44-70 L 30-55	"It is difficult to see in any way that definite increase in deafness has accompanied child-bearing."[1]
R. B.	21 in 1936	0		Para 1 Sept. 19, 1936	Sept. 9 R 25-65 L 15-40		Nov. 27, 1936 R 30-60 L 25-50 Oct. 5, 1937 R 25-65 L 20-45	
M. B.	23 in 1938	0		Para 1 Aug. 14, 1938	Jan. 11, 1937 R 5-40 L 5-28		Sept. 24 R 10-40 L 0-35 Jan. 14, 1939 R 10-40 L 10-35	
E. C.	24	-	-	Primipara Oct. 31, 1937		July 7 R 30-75 L 40-75	Feb., 1938 R 40-80 L 40-85	
A. J.	31	-	-	Para 2 Oct. 16, 1932	Dec., 1931 R 10-55 L 17-50		June, 1937 R 25-50 L 20-50	

[1]Bunch. C. C.: Laryngoscope 49: 805, 1939.

3. For progressive deafness to be considered as an indication for therapeutic abortion a definite diagnosis of otosclerosis must first be made.

4. Definite otological evidence should be obtained and preserved before, during, and following pregnancy and lactation for evaluation concerning succeeding pregnancies.

5. Otosclerosis should probably not contraindicate marriage or a trial pregnancy.

6. Otosclerosis should not be considered as an indication for therapeutic abortion in the primipara.

7. A familial history of deafness need not be present but may be one of the deciding factors in the decision for interruption of pregnancy. We believe that a multiparous woman may have considerable right to question the continuation of her pregnancy if accurate otological evidence obtained in previous pregnancies has shown a marked, *sustained*, loss of hearing.

8. Before therapeutic abortion is decided upon, the patient should be informed that otosclerosis is a progressive disease, even without pregnancy; also that hearing aids and lip reading offer great help.

9. Fetuses in all stages of development born to mothers with decreased hearing should be preserved for examination by a competent otological pathologist. This is especially true of twin pregnancies.

I wish to express my great appreciation to the many otologists and obstetricians whose names are included in the above tables who have helped me in the preparation and compilation of this manuscript.

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Discussion

DR. BAYARD CARTER, DURHAM, N. C.—Dr. Allen has given a comprehensive survey of the literature which shows that otosclerosis in females constitutes 66 to 79 per cent of reported case records. He also shows how the problem of otosclerosis of pregnancy was approached in Germany and France. In Germany, the treatment of the disease in pregnancy was based upon political ideology, i.e., race betterment; in France, the treatment was based upon the religious concept. Medical care of the patients, therefore, has been tinted with one of these concepts.

A reading of this paper also shows the confusion existing concerning etiological ideas of the disease. That the disease may be caused or aggravated by head colds, faulty diet, poor teeth, faulty metabolism, puberty, by pregnancy and lactation, menopause, by total sterilization and by mental disease, is considered in the review. The validity and nonvalidity of hereditary studies are also discussed. The author advances the theory that the high estrin levels which occur during pregnancy may affect the hearing by their effects upon the mucous membrane of the ear in a manner similar to the action of the high estrin levels on mucous membranes in other parts of the body. This theory is an arresting one and worthy of serious consideration.

Dr. Allen also expresses clearly the criteria for diagnosis, i.e., progressive deafness, Bezold's triangle, normal middle ear and eustachian tube. He rightly emphasizes the necessity of audiometer measurements of the loss or gain in hearing to make case records reliable and complete.

Our experience with otosclerosis in pregnancy is based upon the study of two patients. One of these patients had a complete and comprehensive work-up and one had incomplete study.

PATIENT 1.—Aged 23, para 0-0-0. The mother of this patient was deaf. The patient herself was "hard of hearing from 13 years of age and the diagnosis of otosclerosis was made prior to marriage." This patient presented herself with a pregnancy of eight weeks. She and her husband were highly intelligent and asked advisability of abortion. This we declined to do and explained that the advantages of children, who would probably not have otosclerosis, would far outweigh an increase in her deafness.

The first pregnancy, 11 years ago, was normal in every way and the child was normal. The audiometer tracing, however, showed a decrease in hearing.

The second pregnancy, eight years ago, was also normal, but the audiometer tracing again showed a decrease in hearing.

The third pregnancy, seven years ago, ended in a spontaneous abortion at ten weeks without change in audiometer tests.

The fourth pregnancy was also normal in every way. The audiometer tests showed decreased hearing with tinnitus accentuated. This patient was last seen 15 months ago.

PATIENT 2.—Aged 36, para 9-2-7. This patient, who had noticed increasing deafness after her fourth pregnancy, was admitted for intrapartum bleeding. A spontaneous delivery and uncomplicated puerperium followed. She left the hospital against advice on the sixth day, before audiometer tests could be undertaken. A letter from the patient reported hearing "just as bad as ever but no worse."

Dr. Allen's presentation should arouse interest concerning deafness in pregnancy and the survey as conducted by him establishes data of real clinical value.

DR. WILLARD R. COOKE, GALVESTON, TEX.—While otosclerosis is somewhat rare, to the patient concerned it is of vital importance. It behooves us not to neglect the thorough study of every case in which the disease is known to exist in the individual or in the family, or in which the rather frequently encountered symptoms of tinnitus or diminished acuity of hearing develop during pregnancy.

As a personal contribution, I can cite only two cases and a family record covering four generations. In one of the cases, no subjective change occurred during or within three years after pregnancy. In the other, the disease was markedly progressive during pregnancy without subsequent regression. The family record is as follows: The first known case occurred in the great-grandmother of the present youngest generation. Of two sons and a daughter, the daughter only was affected. The disease has not occurred in the descendants of the sons. The daughter had two sons and two daughters, one of each being affected. Neither daughter had children, and in the six children, now aged 26 to 35, of the two sons the disease has not yet appeared.

DR. FRED L. ADAIR, CHESTERTON, IND.—It seems to me that we must base our decisions on the termination of pregnancy for otosclerosis on some definitely defined ideas about abortion in general. One has to recognize in setting up indications for abortion, first the effect on the mother, and second the possible effect on the fetus in allowing the pregnancy to go on to term. Hereditary aspects are probably a factor in the condition, but the hereditary trend is certainly not 100 per cent. Are we justified in therapeutic abortion when the hereditary factor does not involve 100 per cent of the fetuses? In other words, if we do a therapeutic abortion where the hereditary factor might produce 50 per cent or less of defective offspring, we would run an even chance of destroying a normal fetus, or one which might have some defect later.

Second, are we justified in doing a therapeutic abortion where the fetus if it survives and develops the hereditary condition, though handicapped, can still lead a useful existence? In setting up an indication for therapeutic abortion that should be given serious consideration.

With regard to the mother, it is uncertain whether or not the continuation of the pregnancy really has a serious effect on the course of the disease. It certainly does not have a serious effect in all mothers. In some cases we do apparently have a temporary exacerbation of the disease which in some patients disappears after the pregnancy is over. We have difficulty in predicting in advance what effect pregnancy may have in a given case.

Then we also have to consider the very serious ethical question of whether or not some handicap to the mother, which does not interfere with her living a useful though handicapped life, justifies destroying another life which could be a perfectly normal individual.

We have to be extremely careful in setting up indications for therapeutic abortion, which get into the literature and are difficult to eradicate. This is particularly

true for conditions about which we are not clear in our own minds as to their hereditary character or their response to pregnancy. Dr. Allen's contribution has been extremely sound and sane, for this is a condition of considerable interest to the obstetrician because of the attitude of a considerable number of patients toward the condition of the child and toward their own impaired hearing.

DR. CURTIS F. BURNAM, BALTIMORE, MD.—I have had the opportunity through the Otolaryngological Department of the Johns Hopkins Hospital to consult with Dr. Samuel Crowe about the cases of clinical otosclerosis occurring there. Apparently, it is a rare disease but otosclerotic pathological changes in various parts of the temporal bone are extremely common, and where they made serial sections, a very high percentage of those bones showed the lesion. If the stapes is not involved, there is no change in hearing, and these changes have no clinical significance. Heredity, while a factor, does not justify clinical abortion, nor does the possible increase in deafness in the mother justify this procedure.

DR. JOSEPH L. BAER, CHICAGO, ILL.—Dr. Allen's note of warning brought to my mind a patient who, following her first pregnancy, had lost approximately one-third of her hearing capacity in both ears, and who deliberately embarked upon a second pregnancy, having been told that there was a distinct likelihood of further impairment of her hearing. Following the second pregnancy, she had lost two-thirds of her hearing and was resorting to mechanical devices. She and her husband consulted with me concerning the advisability of a third pregnancy. I pointed out that it might terminate in complete deafness, which opinion was confirmed by the otologist. Nevertheless, she deliberately embarked upon a third pregnancy and did, in fact, lose almost her entire hearing perception. Now if she had inadvertently become pregnant on this third occasion and had appealed to me for termination of that pregnancy, because of what had happened previously, I would have had no hesitation about performing a therapeutic abortion and sterilization.

DR. ALLEN (closing).—I have nothing to add except in replying to the question about the diagnosis of otosclerosis by x-ray. My otological friends have made it very plain to me how difficult it is to make a definite diagnosis by the ordinary tests, and in all the literature I have read I have seen no mention of diagnosis by x-ray.

A THERAPEUTIC REGIMEN FOR ECLAMPSIA*

Based on a Personally Conducted Series of 142 Consecutive Cases Without a Maternal Fatality

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ECLAMPSIA still constitutes a major obstetric problem. Its incidence and mortality rate, although they vary throughout the country, remain on the average appallingly high. It was responsible for more than a third of the total maternal deaths in the six state hospitals of Louisiana during 1943, and the case fatality in the 161 cases treated in these institutions during that year was approximately 10 per cent (16 deaths).

As far as I am able to ascertain from the voluminous literature, the 142 consecutive cases of eclampsia which I am reporting in this communication constitute the largest single series on record without a fatality. The material consists of 120 cases of eclampsia treated under my personal supervision and direction at Charity Hospital of Louisiana at New Orleans during the five-year period ending January 1, 1944, and of 22 cases treated during 1941 at the Pineville Charity Hospital, with the cooperation of Dr. John W. Williams. As there are no essential differences in the material, it will hereafter be analyzed as a unit.

Although, as already stated, these cases were treated under my personal supervision and direction, their uniformly successful outcome is due to the enthusiasm and warm cooperation of the visiting and resident staffs of Charity Hospital, including Dr. Frank J. Bertucci, Dr. William F. Guerrero, Dr. Daniel W. Goldman, Dr. Ben L. Lehman, Dr. Roland F. Phillips, Dr. Stephen L. Watson, and Dr. John W. Williams, the latter of whom later transferred to the Pineville Charity Hospital. I am happy to acknowledge their share in this work, which many times required the continuous observation of patients, sometimes by several members of the staff, for hours on end. Such observation, as I shall point out later, had much to do with the successes achieved.

All of these cases were treated by the same general, essentially conservative plan, which was, however, modified to meet the circumstances of every individual case. We are convinced that the universal adoption of a similar individualized but essentially conservative therapeutic regimen would materially reduce the general mortality in this disease. A review of the recent literature supports the point of view that the therapy of eclampsia is still unsettled. The chief point of similarity

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

in the various plans now advocated is that they tend to be less radical than they formerly were, but there, as a rule, resemblances end. My own experience with interns, residents, postgraduate students and even practicing physicians has convinced me that this lack of agreement on the part of obstetric authorities results in confusion and experimentation among inexperienced men, many of whom, although well taught, seem inclined to regard eclampsia as an etiologic problem rather than as a clinical condition in which two lives are the stake. Personally, I have no doubt that this state of confusion contributes heavily to the general mortality of the disease.

Analysis of Material

The principal object of this communication is to outline a plan of therapy for eclampsia, the effectiveness of which has been demonstrated in the series of cases under consideration. The use of special personal records in these cases, however, in addition to the usual hospital records, has resulted in the accumulation of considerable other data of interest, which will be briefly summarized.

Incidence.—During the five-year period in which these 142 cases were treated, the incidence of toxemia of all degrees and types in the wards in my charge was 8.12 per cent, and eclampsia represented 13.1 per cent of all the toxemias observed. This relatively high proportion is chiefly explained by the fact that as a rule only severe cases of toxemia reach the hospital from distant areas. Patients with mild degrees seldom leave rural areas for medical attention, and do not always seek it even if they live in the city. It should be added, however, that approximately 75 per cent of all patients now delivered in the New Orleans Charity Hospital have received prenatal care in the hospital clinics.

The incidence of eclampsia on my service during this peroid was 1.07 per cent, the ratio being 1:93.3 viable obstetric admissions. The ratio varied from 1:98 in 1939 to 1:103 in 1943. It was 1:94 in 1940, 1:79 in 1941, and 1:105 in 1942. Failure to demonstrate a uniformly declining incidence curve is not altogether discouraging, for it is to be explained by improvement in hospital facilities, as the result of which patients from distant areas are now adding materially to local statistics. Approximately 60 per cent of the patients in this series resided outside of the city limits, and 12 per cent lived more than 50 miles away.

The marked disproportion in the racial incidence (114 colored to 28 white patients) is more apparent than real, since the incidence rate of eclampsia, based on obstetric admissions, was almost the same for the two races (1.05 per cent colored, 1.08 per cent white). Comparisons on the basis of race are frequently interesting and valuable at the New Orleans Charity Hospital, but in eclampsia we have observed no inherent racial variation effective in influencing either the susceptibility to, or the severity of, the disease. We have also observed no difference in eclampsia as exhibited in rural and urban Negro women, or in southern and northern Negro women.

This series bears out the common observation that eclampsia is definitely a disease of young primiparas. Although the age range was

from 13 to 41 years, 71 per cent of the patients (101) were less than 21 years of age. Although the parity ranged from one to 10 pregnancies in the 26 multiparas in the series, 81.2 per cent of the patients (116) had not previously been pregnant, and only four patients had had more than two pregnancies. On the other hand, the disease tended to be more severe in older women and in multiparas, probably because repeated childbearing had lowered resistance and initiated tendencies to chronic vascular or renal disease.

Eclampsia is most likely to occur in the third trimester of pregnancy. In one case in this series it developed at 26 weeks, in another at 28 weeks, and in a third at 30 weeks, but 38 per cent of all cases occurred between the thirtieth and thirty-sixth weeks, and 60 per cent between the thirty-sixth and fortieth weeks.

Possible Etiologic Factors

Special studies were made of certain factors to determine their possible etiologic significance. In this series, as in all other reported series, convulsions were usually precipitated in susceptible cases by such generally recognized stimuli as anger, worry, overwork, lack of sleep, the irritation of examinations and other manipulations, or the stress and strain of labor and delivery. No fundamental emotional instability, however, was evident in any patient. As a matter of fact, when once the stage of acute toxemia had been controlled, these women, as a rule, seemed to be rather more stable emotionally than are the average pregnant women.

Meteorological Environment.—In some instances, particularly of antepartum eclampsia, there was no apparent reason for the abrupt onset of the attack. Our own experience, like that of other obstetricians, is that eclampsia tends to occur in groups of cases, after long intervals without a case. Recently, for instance, following an interval of six weeks without a single case, seven women with eclampsia were admitted within 30 hours to three state hospitals located within a radius of 150 miles. Intrinsic or extrinsic factors would scarcely operate simultaneously, and chance coincidence seems an unlikely explanation.

Since local atmospheric changes seem to furnish the only obvious common factor in such circumstances, an investigation from this standpoint was undertaken in all cases of antepartum eclampsia in this series. Through the cooperation of the U. S. Weather Bureau in New Orleans, meteorograms made at the time of onset of the seizures were studied in these cases, and it was found that in 83 per cent (62 cases) the onset coincided with a rising barometric pressure, a decreasing environmental temperature, and a high degree of humidity. In six instances tropical electrical storms were also present. We have, of course, no intention of claiming that the weather is of etiologic significance from the standpoint of the disease itself, but the speculation seems reasonable that abrupt changes in the physical milieu sometimes may require physiologic adjustments beyond the capabilities of abnormal individuals.

Protein Deficiencies.—Dietary investigations carried out in the last 62 cases in this series suggest that protein deficiencies may be of etiologic significance in eclampsia. Certainly these studies discredit still further

the belief, which is still held in some quarters, that high protein consumption is a cause of eclampsia and that limitation of the protein intake may prevent it.

Not one of these 62 patients had an optimum protein intake (1.5 Gm. per kg. of body weight per day) and only three had an intake above the minimum subsistence level (0.75 to 0.90 Gm. per kg. per day) for the last trimester of pregnancy. The range of intake was from 0.20 to 0.92 Gm. per kg. per day, and approximately a third of the protein ingested was derived from cereal and vegetable sources and was therefore of low biologic value. In many instances, inadequacies which had apparently existed over long periods of time were aggravated during pregnancy by restriction of meat, eggs and milk, either self-adopted or carried out on medical advice. Protein deficits were also increased by such obvious causes as vomiting, frequent catharsis, and proteinuria.

Serum protein determinations made during the eclamptic stage in 47 patients showed an average concentration of 5.10 ± 1.10 Gm. per cent, in spite of hemoconcentration at the time, which is definitely lower than the normal average (approximately 6.5 Gm. per cent). A rough correlation existed between the degree of edema and the serum albumin level, but otherwise it was not possible in the individual case to correlate the serum protein level or the degree of edema with the protein intake, or to correlate this level with the degree of edema.

Cerebral Dysrhythmia.—Electroencephalographic studies on 26 patients who had had eclampsia from two days to four and a half years prevoiusly revealed abnormal findings in only three, 11.5 per cent, which is approximately the incidence of abnormality likely to be found in any series of similar tests on apparently normal individuals. The patient who had had eclampsia two days before, and the patient who had had eclampsia in two successive pregnancies were both normal. The findings thus do not support the theory that eclamptic subjects may suffer from a primary cerebral dysrhythmia, which may be exaggerated to the convulsive degree by a "trigger mechanism" in the form of the associated toxemia.

Convulsive Diathesis.—The familial tendency to eclampsia postulated by certain observers on the basis of small numbers of observations is not borne out by this study. Four of the 26 multiparas in the series had previous histories of toxemia. One patient had eclampsia in 2 successive pregnancies during the period of observation, 1 had a previous history of eclampsia, and 2 had had severe pre-eclamptic toxemia in previous pregnancies. The apparent rate of repetition, however, 16.6 per cent, decreases to 6.7 per cent when the 60 pregnancies in these 26 women are taken into consideration. Excepting the two instances of eclampsia, not a single patient gave a history of previous convulsive disorders of any kind.

The family history is complete in only 46 of the 142 patients. The mother of one patient and the sister of another had had eclampsia, and the brother of a third patient suffered from epilepsy. It is a matter of interest, however, that twin sisters of two of the eclamptic subjects were normal, as were the families of the two patients with recurrent eclampsia. The family history was thus positive in only 6.5 per cent of these 46 cases, and even when the two patients with a personal history of recurrent eclampsia are added to the group of positive subjects, the familial incidence rises to only 10.8 per cent.

The constitutional build of eclamptic subjects seems to play some part in the development of the disease, although our observations on this point are incomplete. The weights of 68 patients as determined at the first postpartum visit ranged from 88 to 263 pounds. Several weighed less than 100 pounds, but the average weight was 145 pounds, and 17 weighed more than 160 pounds. Quite aside from statistical data, we, like others, have learned to treat with particular respect the thick-necked eclamptic subject of short stocky build.

Complications of Pregnancy.—Complications and abnormalities were frequent in this series, though whether they were causal or merely coincidental it is not possible to say. Seventeen patients had syphilis and 2 had fibroids, which is about the usual incidence for these conditions on the obstetric service. Eight patients exhibited severe anemia, in one instance of the sickle-cell variety. Eleven patients (7.7 per cent) had pyelitis, which is approximately three times the clinic average. Fifteen (10.5 per cent) had hyperemesis gravidarum, which is 10 times the average. Eight (5.6 per cent) had repeated periods of vaginal bleeding, which is several times the clinic average. There were 7 sets of twins in this series, a ratio of 1:20.3, which is 4 times the average rate and which substantiates the common observation that eclampsia is unusually frequent in multiple pregnancy.

Classification and Grading

In 104 of these 142 patients, 73 per cent, convulsions began prior to delivery, and in 74 cases, 52 per cent, labor had not yet begun. Doubtful cases were classified as intrapartum if delivery occurred within 12 hours of the first convulsion. The incidence of postpartum eclampsia is unusually high because 12 patients were admitted in convulsions after delivery outside of the hospital.

If therapy is to be evaluated with any degree of accuracy, eclamptic patients must be graded on the basis of severity, as well as classified as to time of occurrence. For grading purposes we prefer the criteria proposed by Dieckmann, which are based on the presence of one or more of the following findings: (1) more than ten convulsions; (2) coma; (3) hyperpyrexia; (4) pulse rate over 120 per minute; (5) respiratory rate over 40 per minute; (6) cardiovascular impairment; (7) failure to respond to treatment. On the basis of these criteria (Table I), 52 patients (36.6 per cent) were classified as having severe grades of eclampsia. The proportion of severe grades was only about a third as high in the delivered as in the undelivered groups, but was much higher in multiparas than in primiparas (54 and 33 per cent, respectively).

TABLE I. CLASSIFICATION OF 142 CASES OF ECLAMPSIA

TYPE	NUMBER	PER CENT	GRADE			
			MILD		SEVERE	
			NUMBER	PER CENT	NUMBER	PER CENT
Antepartum	74	52.1	40	54.0	34	46.0
Intrapartum	30	21.1	18	60.0	12	40.0
Postpartum	38	26.8	32	84.2	6	15.8
Total	142	100.0	90	63.4	52	36.6

Such grouping, though very useful, is sometimes difficult and is frequently inaccurate, for patients who present apparently identical manifestations may actually be quite dissimilar in their reactions to the disease. One patient, for instance, without ever seeming very seriously ill, may recover in spite of a dozen or more convulsions, oliguria, hyperpyrexia, and very rapid pulse and respiratory rates, while another may seem critically ill in the absence of most or all of these manifestations. When tangible as well as intangible factors are taken into consideration, the incidence of severe grades of eclampsia in this series rises from 36.6 to 44 per cent.

The number of convulsions ranged from one to 22, and 19 patients (13.4 per cent) had more than 10. Although the number is generally an index of the severity of the disease, one patient in this series who had 22 convulsions delivered a live baby and has presented no abnormal sequelae.

Experience with many patients whose lives were jeopardized by severe pre-eclamptic toxemia has caused us to speculate on the possibility that convulsions may sometimes form an actual protective or release mechanism which guards against even greater dangers. Not infrequently, toxemic patients appear in better condition and seem more easily managed following a short seizure than before it occurred. Furthermore, critically ill toxemic subjects with no tendency to convulsions may present greater residual damage than true eclamptic subjects. This reasoning is in line with the accepted fact that eclampsia without convulsions is the most dangerous type of the disease. Paradoxical as the theory seems, it is not incompatible with accepted explanations of other defense mechanisms, such as the development of fever and leucocytosis in infection and of hypotension and shock in ruptured ectopic pregnancy.

Plan of Therapy

The plan of therapy outlined in this paper is based not only on our experiences in the 142 cases reported herewith, but also on a personal experience of approximately 250 other cases which have come under my observation in the past 14 years. The basic principles have been evolved gradually, but have not been changed substantially in the last two years.

There is nothing new or original about this therapeutic regimen. The various steps have been proposed by others and are well known. Many have secured excellent results with them. Others have failed, chiefly, we believe, because the treatment is superficially simple and unspectacular, as well as exceedingly tedious, and as a result two precautions to the strict observance of which we attribute much of our success are likely to be omitted:

1. Constant (in the most literal sense of the word) observation of each eclamptic patient by an experienced staff throughout the entire course of treatment, which permits

2. Careful integration of the various therapeutic components into an individualized regimen rather than their application as a standard routine of treatment.

The basis of the whole regimen is an ultraconservative concept of management, in which the dangers of overtreatment and indiscriminate treatment as well as those of undertreatment are evaluated.

The outline of treatment which follows is deliberately detailed and may seem unnecessarily so in comparison with other plans in which some special phase of therapy is stressed. We regard strict attention to details, however, as fundamental to success, for, as already pointed out, individual differences among patients make routine orders unsafe and continuous observation mandatory, in order to determine the changing indications for therapy. It is impossible to outline a safe treatment for the entire course when the patient is first seen, and seldom possible prior to delivery.

For clinical purposes, the therapy of eclampsia is best planned according to the stage of the disease. For this purpose eclampsia may be arbitrarily divided into the following stages, which may vary widely or be absent and all of which, for obvious reasons, occur only in antepartum eclampsia:

1. *The Convulsive Stage.*—This is the interval from the onset of convulsions to their complete control. It is characterized clinically by convulsive seizures, by hyperirritability alternating with coma, and by stupor and disorientation.
2. *The Postconvulsive Stage.*—This is the interval between the final convulsion and the return of full consciousness. It is characterized clinically by coma, semicoma and restlessness, but convulsions are absent.
3. *The Controlled-Eclamptic Stage.*—This is the interval of convalescence and improvement between the postconvulsive stage and the onset of labor. There may be during it an occasional abrupt recurrence of fulminating symptoms, but it is usually characterized by definite amelioration or complete disappearance of acute toxic manifestations.
4. *The Posteclamptic-Parturient Stage.*—This stage includes the period of labor and delivery.
5. *The Posteclamptic-Postpartum Stage.*—This is the period between delivery and the patient's discharge from the hospital.

Although only five formal stages of eclampsia are recognized, it is well to emphasize at this point that the eclamptic woman should be observed for a long period in the postpartum clinic and should not be discharged from observation during the remainder of her life. Adequate supervision and care are particularly essential during subsequent pregnancies.

The Management of the Convulsive Stage

Antepartum eclampsia naturally is the most difficult to manage because the problem of termination of pregnancy is added to the purely medical problem involved in the eclamptic state. For this reason, the plan of management which follows deals primarily with this type; the same principles, however, are applicable to all types.

In the convulsive stage the following measures are employed:

1. *General and Special Measures.*—The patient is put to bed in a quiet, darkened room and medical and obstetric examinations are, so far as possible, deferred until sedation has become effective, since even apparently insignificant manipulations may precipitate further convulsions.

During convulsive periods and periods of coma the patient is protected against falls and other injuries, preferably by bed guards or side boards. We have observed two instances of cerebral concussion and one of intracranial hemorrhage, as well as several serious contusions and lacerations, because these simple precautions were omitted. Forcible restraints, however, are highly irritating and should never be employed.

False teeth, rings, bracelets and other jewelry are removed at once. A mouth gag is inserted, with due care that neither the patient nor the attendant is injured in the process. We have observed serious hemorrhage from lacerations of the tongue and lips because this precaution was omitted. If the tongue falls back and interferes with breathing it is pulled well forward, and, if necessary, is held in that position.

The patient's position in bed is important. Pillows are not used, but the head of the bed is elevated unless pulmonary edema is so extreme as to demand postural drainage by elevation of the foot of the bed. At least once each hour the entire body is gently shifted from one position to another. A suction apparatus with attached catheter is employed without delay to aspirate vomitus, blood, mucus, and fluid originating in pulmonary edema. Pure oxygen is administered by continuous flow through a nasal catheter or, if cyanosis is marked, by means of a mask. These measures, all of which promote respiratory ease, will usually prevent such common pulmonary complications of eclampsia as respiratory distress, cyanosis, inspiration atelectasis, pneumonitis, pneumonia, and, above all, pulmonary edema.

The blood pressure cuff is kept continuously on the arm and the blood pressure is determined hourly until convulsions and coma are completely controlled. A retention catheter is inserted in the bladder and the urinary volume is determined hourly. The catheter is also inspected regularly for possible leaks or kinks and is irrigated every four hours to prevent obstruction by pus or by precipitates of protein, which frequently accompany or follow periods of oliguria or anuria.

The blood is typed as soon as possible, since transfusion may be required at any time to combat anuria, shock developing from vascular collapse, hemorrhage from abruptio placentae or placenta previa, postpartum hemorrhage, or any other of the complications not infrequently associated with eclampsia.

2. *Sedation to Control Convulsions.*—As soon as the patient is admitted to the hospital, morphine sulfate gr. ¼, and sodium phenobarbital gr. 5, are given subcutaneously. Fifteen minutes later, if convulsions are still present or if hyperirritability is extreme, she is also given 20 c.c. of 10 per cent magnesium sulfate solution, which is injected slowly into the vein. In our experience intramuscular injection is less effective than intravenous injection.

Magnesium sulfate sometimes has a favorable effect on cerebral edema and may stimulate urinary output. If in spite of these measures severe convulsions persist, as they occasionally do, sodium amytal is given intravenously in doses of 3 to 6 gr., or morphine is repeated in doses of ⅛ to ¼ grain. Magnesium sulfate is not repeated unless convulsions recur

or seem imminent, possibilities which are guarded against by continued sedation, usually in the form of sodium phenobarbital (gr. 1.5 to 5, as necessary to control restlessness).

It will be observed that we use all sedatives in very small doses and that we limit the list, as far as possible, to morphine, sodium phenobarbital, and magnesium sulfate. This is intentional. Sedatives are administered in the smallest amounts sufficient to terminate convulsions, prevent their recurrence, and control extreme irritability, on the principle that deficits in sedation can be rapidly and easily corrected, but that oversedation cannot be withdrawn.

The rationale of strict limitation of sedation is clear. Our own observation of eclamptic cases in which heavy sedation is used is that the blood pressure is lowered to dangerous levels; anoxemia, anoxia and acidosis are aggravated by diminution of respiratory activity; the tendency to cerebral and pulmonary edema is increased; stupor and coma are accentuated; and the urinary output is decreased. As a result, patients in profound drug stupor may develop serious complications, which may prove resistant to therapy. Heavy sedation also affects the child adversely.

A second reason for using a limited number of drugs, and those in small quantities, is the considerable variation both in eclampsia and in the individual patient's idiosyncrasy to drugs. A third is that there may have been a previous administration of drugs in the home, on the way to the hospital, or in the admission room, which for various reasons may not be realized until later. We have seen patients remain in profound stupor for as long as 96 hours, apparently from the cumulative action of various drugs administered at short intervals.

The principles outlined were applied in the 142 cases in this series. Fifty-five patients (32 per cent) received only morphine and sodium phenobarbital, and 76 (54 per cent) also had one or more injections of magnesium sulfate. Only 12 patients (14 per cent) had sodium amytal, always in small doses, and this drug was used only twice in the last 51 cases.

The success of these measures is evident in the rapid and complete control of convulsions achieved by them. Forty per cent of the patients (57) in this series had no more convulsions after treatment had been instituted, while 34 per cent (48) had only one more (Table II). Within 30 minutes after treatment had been started, convulsions were permanently controlled in more than half the patients (Table III). Response to therapy was usually most rapid in postpartum and least rapid in antepartum eclampsia, but in no instance did patients in the antepartum

TABLE II. RESPONSE OF CONVULSIONS TO THERAPY

	TYPES OF ECLAMPSIA						CUMULATIVE PER CENT
	ANTEPARTUM		INTRAPARTUM		POSTPARTUM		
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	
None after institution of treatment	20	27.0	3	10.0	34	89.6	40.1
One convulsion	33	44.6	12	40.0	3	7.8	73.9
Two convulsions	5	6.8	11	36.7			85.2
Three convulsions	5	6.8	3	10.0			90.8
Between 3 and 5 convulsions	7	9.4	1	3.3	1	2.6	97.1
Between 5 and 10 convulsions	3	4.0					99.3
More than 10 convulsions	1	1.4					100.0
Total cases	74	100.0	30	100.0	38	100.0	

group have recurrences of their convulsions after delivery. Such recurrences as did develop came on early and suddenly, but were usually mild and of short duration.

TABLE III. TIME REQUIRED TO CONTROL CONVULSIONS

	TYPES OF ECLAMPSIA						CUMULATIVE PER CENT
	ANTEPARTUM		INTRAPARTUM		POSTPARTUM		
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	
None after institution of treatment	20	27.0	3	10.0	34	89.6	40.1
Within 30 minutes	12	16.2	5	16.7	1	2.6	52.8
Within 45 minutes	15	20.3	7	23.3	1	2.6	69.0
Within 60 minutes	9	12.1	9	30.0	2	5.2	83.1
Within 2 hours	10	13.5	3	10.0			92.3
Within 4 hours	3	4.0	2	6.7			95.8
Longer than 4 hours	5	6.8	1	3.3			100.0
Total cases	74	100.0	30	100.0	38	100.0	

3. *Verification of Diagnosis.*—Convulsions, regardless of their origin, can all be controlled by the same therapeutic measures, but additional treatment without an exact diagnosis may end in disaster, for pregnancy plus convulsions does not always add up to eclampsia. We once saw a pregnant woman with diabetic convulsions treated with glucose and another with postconvulsive shock and a ruptured uterus treated as if she were in eclamptic coma, with disastrous results in both cases. The diagnosis of eclampsia can be made with reasonable accuracy in most cases by careful interpretation of the sequence of events as correlated with hypertension, edema, and proteinuria.

During the five-year period of this study, 162 women with convulsions were admitted to our obstetric services in the New Orleans Charity Hospital, but only 120 of them had eclampsia. The remaining 42 patients presented variously:

Epilepsy in 11 cases.

Central nervous system affections in five cases (brain tumor, specific meningitis, arsenical encephalitis, traumatic concussion, and rupture of a syphilitic basilar aneurysm).

Hysteria and diabetes in four cases each.

Reactions to therapeutic measures in four cases (blood transfusion, caudal analgesia, intravenous oxytocic medication, barbiturate analgesia).

Hematogenous disease in three cases (massive septicemia, massive hemorrhage, hemolytic crisis in sickle-cell anemia).

Chronic hypertensive disease (encephalopathies) in three cases.

Chronic renal disease (glomerulonephritis, pyelonephritis, renal calculi) in three cases.

Food poisoning and drug poisoning in one case each.

Hyperemesis gravidarum, chorea, and tetany and alkalosis in one case each.

4. *Measures to Promote Hemodilution, Diuresis and Detoxification.*—As soon as the diagnosis of eclampsia has been confirmed, 500 c.c. of 20 per cent dextrose solution in distilled water are given by intravenous infusion, the period of administration usually covering about 50 minutes. A patient with evidence of cardiac failure or pulmonary edema receives from 50 to 150 c.c. of 50 per cent solution, and a patient with evidence of dehydration, which may be present in spite of edema, receives 1,000 c.c. of 5 to 10 per cent solution. If the initial injection fails to stimulate

a satisfactory urinary output, the concentration of the solution is increased and the volume is decreased, but infusions are seldom given oftener than every four hours. If the urinary output at the end of four hours has averaged less than 25 to 30 c.c. per hour, an infusion of 300 c.c. of 30 per cent dextrose solution is given. Thus the intravenous administration of dextrose is carried out in all cases only during the period the patient is unable to take sufficient fluids by mouth, and it is discontinued if it is clearly producing no results.

Although the value of intravenous injections of hypertonic dextrose solutions in promoting hemodilution and diuresis has long been established, it is our custom to use them only on strict indications. They are employed chiefly during the convulsive stage, and they are limited to the smallest amounts which will produce a urinary output of 25 to 30 c.c. per hour. The injudicious use of large quantities of fluid may result in cardiac embarrassment and serious acute pulmonary edema, and will aggravate an already impaired water balance if there is little or no urinary output, particularly if the patient is heavily sedated.

Persistent oliguria or anuria associated with such conditions as anemia, hypoproteinemia, or hypotension due to vascular collapse or hemorrhage, demands special additional measures. Anemia and hypotension are treated by blood transfusions. Hypoproteinemia without anemia is treated by plasma transfusions. Patients who continue oliguric or anuric in spite of these measures are treated by diathermy over the kidney regions and are also given 1,000 c.c. of sodium sulfate (4.285 per cent) by vein, followed in four hours by the intravenous injection of 50 c.c. of 50 per cent dextrose. In 16 cases in this series, 9 of which were instances of intrapartum eclampsia, anuria developed for periods ranging from 8 to 31 hours.

Only 7 of the 142 patients did not receive dextrose. Seventy-five (53 per cent) received only 20 per cent solutions, but 39 (27 per cent) also received 30 or 50 per cent solutions, and 21 (15 per cent) required infusions of 5 to 10 per cent solution in addition to the higher concentrations before a satisfactory urinary output was established. Sucrose was used in four of the early cases in this series, but was discontinued, in spite of apparently satisfactory results, on the basis of reports from elsewhere of hemorrhagic nephritis following its use. Twenty-three patients (16 per cent) received blood transfusions, which in one instance amounted to 2,850 c.c., 4 received plasma transfusions, and 7 received sodium sulfate solution.

5. *Special Therapeutic Measures.*—If marked cerebral irritation is evident, in spite of sedation and intravenous dextrose therapy, spinal drainage is carried out. We have found this measure of some value, particularly in postpartum eclampsia, in the reduction of intracranial pressure due to spasm, edema or hemorrhage, as well as in the verification of the diagnosis of hemorrhage, but we are opposed to it as a routine. Spinal drainage was employed in 12 patients in this series, in 4 of whom it was used twice, and in 1 of whom it was used three times. We are also opposed to venesection, even in the presence of pulmonary edema.

Although in the presence of acute cardiac failure drugs of the digitalis group are theoretically of at least temporary value, we have found them of no particular benefit in the few cases in which we have used them. Toxemic subjects are unusually sensitive to them, and the vomiting which often follows their administration is undesirable. We do not use mercurial diuretics, nor do we use vasodilator drugs such as veratrum viride, the nitrites, and nitroglycerin.

The Management of the Postconvulsive Stage

The coma or semicoma which follows the final convulsion usually passes over imperceptibly into a period of stupor and lethargy, punctuated with episodes of hyperirritability and ending in gradual clinical improvement. It is only occasionally possible to demonstrate the limits of the convulsive and the postconvulsive stage because both control of convulsions and clinical improvement must be demonstrated by developments. Although too little attention is, as a rule, given to it, the postconvulsive stage is not free from danger in itself, and its dangers are increased by the too free use of hypnotic drugs and the induction of labor immediately after convulsions have ceased. The latter error, which is based on the belief that the control of convulsions is equivalent to the control of eclmapsia, is a common and very dangerous mistake.

The following measures are employed in sequence during the postconvulsive stage:

1. *General and Specific Measures.*—Constant observation is continued and a quiet, restful environment is maintained. The use of nasal oxygen is continued, and material is aspirated from the throat when necessary, though the same object can be achieved in a conscious subject by instructing her to cough at frequent intervals. The head of the bed is further elevated and the height is changed at frequent intervals. This simple measure seems to improve cerebral circulation. If the patient is still unable to move about herself, her position is changed by an attendant.

Blood pressure and urinary output are determined at hourly intervals, as during the first stage, but in the absence of special indications other clinical information is obtained at four-hour intervals. As soon as is feasible in this stage, a thorough obstetric examination is concluded.

To hasten detoxification a large dose of magnesium sulfate is given by mouth; and is followed in four hours by a cleansing enema.

2. *Sedation and Administration of Fluids.*—Sodium phenobarbital in doses of 1.5 to 3 gr. is given at three- to six-hour intervals, which is usually sufficient to prevent the recurrence of convulsions. Spastic twitchings, particularly of the fingers and eyelids, often precede convulsions and indicate the need for additional sedation, but some degree of restlessness is to be expected, and bodily movements per se, should not be regarded as abnormal. If considerable cerebral irritation is evident, intravenous magnesium sulfate should be repeated as necessary, but in this as in the first stage all sedation is limited.

The continued use of intravenous hypertonic dextrose solutions may be necessary early in this period, but as a rule fluids can be given orally, especially if sedation is limited. In the eclamptic woman, just as in normal individuals, a larger urinary output is stimulated by oral than by parenteral fluids. As soon as the swallowing reflex has returned, a minimum of 200 c.c. of highly sweetened fruit juice is given each hour, it being the duty of the nurse or physician to administer it as regularly as if it were a prescribed medication. Water, coca cola, milk, coffee, tea or beer may be taken as desired. Many patients will take several times the minimum required amount of fluid, and should be encouraged to take as much as they comfortably can, though fluids should not be

pushed to the point of nausea. Copious diuresis and clinical improvement are frequently observed a few hours after the oral intake of fluids is begun, even in patients whose response to parenteral dextrose therapy has not been satisfactory.

The Management of the Controlled-Eclamptic Stage

Toward the end of the postconvulsive and in the first part of the controlled-eclamptic stages, the patient, if the response to treatment has been satisfactory, may be drowsy but she can be roused and she is usually fairly well oriented. Very little sedation is required, and she is taking large quantities of fluids by mouth. The gastrointestinal tract is clean. The blood pressure is stabilized in the range between 150 and 170 systolic, and the pulse pressure is approximately normal. Edema disappears slowly. The urinary output, even though diuresis may not be free, maintains a safe relationship to the intake. Proteinuria gradually disappears, at first slowly and then at a more rapid rate. Serial cell volume determinations reveal progressive improvement in hemoconcentration.

There is considerable variation in the rapidity and extent of improvement in the controlled-eclamptic stage. Residual mild headache and visual disturbances may be present early in this stage, but more often the only notable abnormality is some degree of lethargy. Improvement, though usually gradual, is noticeable from day to day, and 4 to 10 days after the attack, the patient's status suggests a mild preeclampsia. Some subjects, indeed, would be considered normal if the history of convulsions were withheld. Sometimes spectacular improvement is seen immediately subsequent to the convulsions and coma, and even when the improvement is gradual many patients are so well that it is difficult to keep them in the hospital.

The therapeutic regimen during the controlled-eclamptic stage is as follows:

1. *Continued Hospitalization and Observation.*—It is imperative that the eclamptic patient remain in the hospital following control of her seizures, and that she remain in bed, though she may move about at will, and may have a back rest.

Continued constant observation during this period is essential. An experienced obstetrician visits the patient at least twice daily, taking time during each visit to review the regular hospital chart and the special toxemia record, and to elicit from the patient herself even apparently minor symptoms. In his absence she is under the continuous observation of a trained nursing and resident staff, the members of which are fully aware of the possibility of adverse changes and of how they will manifest themselves.

2. *Special Diagnostic, Prognostic and Other Examinations.*—Special examinations, which are most conveniently recorded on a special toxemia sheet, include:

Blood pressure determinations at four-hour intervals when the patient is awake, unless there are indications for more frequent determinations.

Accurate volumetric determinations of the daily fluid intake and daily urinary output, which are recorded at eight-hour intervals, since oliguria or anuria may develop rapidly. The patient is weighed daily and the body weight and urinary output are roughly correlated, to estimate the water balance of the body.

Daily qualitative and quantitative determinations of urinary albumin. A sample of the 24-hour volume of urine is used for this purpose.

Microscopic examination of the sediment of a catheterized specimen of urine at intervals of several days.

A daily hematocrit, to determine tendencies toward hemoconcentration or hemodilution. It should be emphasized, in this connection, that because of hemoconcentration hypoproteinemia, with or without anemia, may be overlooked.

Ophthalmoscopic examination as soon as the patient can be disturbed. This examination is repeated at frequent intervals, as changes in the retina often precede changes elsewhere in the body.

Certain special examinations and tests, such as tests of renal and hepatic function, and determinations of venous pressure, circulation time, vital capacity, vascular lability and blood chemical values, as well as electrocardiography, are all interesting, but on the whole, as we have practiced them, they have not supplied consistent or conclusive information. Serial blood chemical determinations, especially of the carbon-dioxide combining power of the blood, the uric acid of the blood and the serum protein concentration may be of prognostic value, but on the whole, are of so little help from any standpoint, that lack of facilities for their determination cannot be accepted as a valid excuse for inadequate treatment of, or poor results in, eclampsia.

3. *Therapeutic Measures.*—Fluids are given entirely by mouth unless some special indication for parenteral dextrose therapy arises. The daily fluid intake is maintained at 4,000 c.c. or over, but patients frequently take much larger quantities without urging, and outputs of 6 to 8 liters per day are correspondingly frequent. A high-protein, salt-free diet is prescribed, which contains 2,000 calories per day and provides approximately 100 Gm. of protein. Supplementary vitamins and minerals are also prescribed.

A saline cathartic is given every third morning. Ammonium chloride in doses of 1 Gm., four times daily, is sometimes helpful if diuresis is not entirely satisfactory. Sodium phenobarbital in doses of 1.5 to 3 gr. is given by mouth to insure sufficient rest at night, but in the absence of indications is withheld during the day. Other hypnotics are avoided, for oversedated patients frequently become irritable and even disoriented, and may complain of headache, nausea and visual disturbances.

4. *Termination of Gestation at the Optimum Time and by the Simplest Possible Method.*—Radical treatment, in which the child is forcibly delivered in the hope of stopping the convulsions, is now universally condemned. On the other hand, it is still common practice, as soon as convulsions are apparently controlled, to induce labor by irritating if not actually traumatic procedures, and to resort to abdominal section if these methods are not promptly successful. This unphysiologic practice, in our opinion, is responsible in no small measure for a definite number of maternal and fetal deaths.

It is to the advantage of both mother and child to defer the termination of pregnancy for a period of time after eclampsia is definitely controlled. From the standpoint of the mother, delay permits the induction of labor with minimum trauma, by progressive gentle stimulation which

results in a normal mechanism of labor, whereas fatalities are not uncommon when induction by bag, bougie or packing is carried out or when cesarean section is performed on a toxic subject. Furthermore, labor often begins spontaneously during the waiting period.

From the standpoint of the child, its chances, like the mother's, are better if recovery from the acutely toxic maternal state is permitted, as well as recovery from the effects of sedation by which that state was controlled. Traumatic procedures, whether for induction of labor or for the purpose of delivery, affect the child adversely. Finally, the nearer the premature child approaches maturity, the better are its chances of life, even though the delay may seem insignificant. The danger of intrauterine fetal death during the period of convalescence has been exaggerated. In this series there were only three such deaths, on the second, third and sixth days following the convulsions. It is possible that these children would not have survived under any circumstances, since their weights varied from 4 pounds, 12 ounces to 3 pounds.

The arguments against the policy of delay are readily answered. It is quite true that even under the most careful regimen there is always danger of sudden recurrence of fulminating toxemic manifestations or of actual convulsions, but this is not frequent. In our own series eclampsia did not recur in a single instance during the waiting period, and in only two cases were signs of their impending return sufficiently serious to demand immediate emptying of the uterus by cesarean section; medical induction had failed in one of these cases.

The danger of permanent damage to the vasculorenal and other systems as the result of delay is also not great. In our own cases, in fact, clinical and laboratory observations revealed such marked improvement, which in some instances amounted to a return to normal status, that we are unable to conceive of the delay as a basis of residual pathology. Furthermore, the incidence of residua found at the follow-up of these patients was no greater in the antepartum than in the other groups. It should be emphasized that this statement covers the group of patients who were delivered more than seven days after the onset of their convulsions, which seems to make clear that intercurrent

TABLE IV. TIME INTERVAL FROM THE FIRST CONVULSION TO DELIVERY

TIME INTERVAL	NUMBER OF CASES	PER CENT
Antepartum Eclampsia		
Less than 24 hours	6	8.1
24 to 72 hours	17	22.8
3 to 7 days	26	35.3
More than 7 days	25	33.8
Average 6.7 days	74	100.0
Intrapartum Eclampsia		
Less than 6 hours	10	33.3
6 to 12 hours	10	33.3
12 to 24 hours	7	23.4
More than 24 hours	3	10.0
Average 7.7 hours	30	100.0
Postpartum Eclampsia		
Less than 1 hour	5	13.2
1 to 6 hours	11	28.9
6 to 12 hours	10	26.3
12 to 24 hours	7	18.4
More than 24 hours	5	13.2
Average 8.5 hours	38	100.0

eclampsia need carry no higher a mortality and no higher an incidence of residua than any other variety.

The longest interval in our series between the onset of convulsions and delivery was 38 days (Table IV). The patient, a 21-year-old primipara, had had seven typical eclamptic convulsions, accompanied by severe hypertension and massive edema; the urine boiled solid. A mild toxemia evident at delivery disappeared within 10 days, and at the last examination, seven months later, there was no trace of any abnormality. Her child, who weighed 3 pounds and 9 ounces at delivery, then weighed 18 pounds.

The added expense of continued hospitalization, the constant care and supervision required, and the anxiety of the patient and her family are not valid reasons for prompt delivery when weighed against possible maternal and fetal salvage, inherent in the more conservative policy.

The policy of watchful expectancy in this series resulted in the spontaneous onset of labor in 42 of the 74 cases of antepartum eclampsia (Table V), the interval from the final convulsion to the onset of labor varying from three hours to 37 days.

If the patient is in good condition and close to term, there is, of course, no contraindication to the prompt induction of labor, which should also be carried out without delay in patients who do not show a satisfactory response to therapy, or who present a relapse which is not promptly controlled. This occurred in 10 cases in this series, though in no instance was it necessary to terminate pregnancy by cesarean section without first attempting induction of labor.

Even under the best of circumstances, however, we do not favor postponing induction indefinitely if labor does not set in spontaneously, for medical induction is not infallible but rather a slow process, often requiring several repetitions of the stimuli, and hurried interference would be undesirable if adverse changes should suddenly occur. Fortunately, toxemia seems to increase the irritability of the uterus, as evidenced not only by the 57 per cent of antepartum cases in this series in which labor occurred spontaneously, but also by the fact that an additional 5 per cent responded to the first attempt at medical induction.

TABLE V. TIME INTERVAL FROM THE FINAL CONVULSION TO THE SPONTANEOUS ONSET OR ATTEMPTED INDUCTION OF LABOR IN 74 CASES OF ANTEPARTUM ECLAMPSIA

TIME INTERVAL	NUMBER OF CASES			TOTAL CASES
	HAVING SPONTANEOUS ONSET OF LABOR	HAVING INDUCTION OF LABOR		
		ELECTIVE	REQUIRED	
Less than 12 hours	8			8
12 to 24 hours	3		2	5
24 to 48 hours	1		1	2
48 to 72 hours	9	1	2	12
3 to 5 days	4	8	3	15
5 to 7 days	6	5	1	12
7 to 10 days	6	3		9
10 to 15 days	2	3	1	6
More than 15 days	3	2		5
	16 days	17 days		
	19 days	19 days		
	37 days			
Total cases	42 (57%)	22 (30%)	10 (13%)	74
Average interval	5.6 days	5.1 days	3.9 days	5.2 days

The simplest method of medical induction is as follows: At 6 A.M. the patient is given 1.5 ounce of magnesium sulfate by mouth, and at 10 A.M. a high hot soapsuds enema is given. At 2 P.M., if no contractions have occurred, 0.5 minim of pitocin is injected subcutaneously. The injection is repeated every 20 minutes, in an amount 0.5 minim greater than the preceding dose, until rhythmic contractions ensue or until a maximum dosage of 3 minims has been obtained. The attempt is repeated every 24 or 48 hours in cases in which the first induction fails, for each attempt, even though unsuccessful, seems to soften and shorten the cervix and to increase uterine irritability until labor finally sets in. We have never observed a serious reaction when pitocin has been used within the limits defined by an experienced obstetrician.

Induction was successful in 16 of the 32 cases in which it was carried out in this series, although 3 patients required 2 inductions, 5 required 3, 2 required 4, and 2 required 5 attempts each. Success was attained within 24 hours in 18 per cent of these cases, within 48 hours in 34 per cent, and within 72 hours in 65 per cent.

When simple measures fail and greater haste seems indicated, as happened in 11 cases in this series, the vagina is liberally cleansed with green soap, after which the cervix is slowly and carefully stretched until it admits at least one finger. The membranes are then stripped from the lower uterine segment. If contractions do not occur within two hours, a course of pitocin is begun. In 4 cases, rupture of the membranes was necessary; in another instance, labor was terminated by cesarean section, because of the presence of a long, firm, closed cervix in a nullipara.

TABLE VI. LENGTH OF LABOR

	TYPE OF ECLAMPSIA — NUMBER OF CASES			PER CENT OF TOTAL CASES
	ANTEPARTUM	INTRAPARTUM	POSTPARTUM	
Less than 4 hours	16		4	15.0
4 to 8 hours	25	2	18	33.7
8 to 12 hours	9	9	5	17.3
12 to 16 hours	8	5	4	12.8
16 to 24 hours	10	5	3	13.6
More than 24 hours	3	4	3	7.5
Delivered by section	3	5	1	6.3
Total cases	74	30	38	
Average time	5.5 hours	13.4 hours	8.6 hours	7.9 hours

The Management of Parturition

Labor was of surprisingly brief duration in most of the 133 patients in the series who were delivered vaginally; the range was from 0.5 to 41.7 hours, but the average was 7.9 hours (Table VI). The longest labors were observed in the intrapartum group, possibly because of the depressing effects of sedation early in labor.

Operative methods of delivery were held to a minimum in order to obviate the ill effects of unnecessary trauma, anesthesia, blood loss and infection in these highly susceptible patients. One hundred nine patients, 76.8 per cent of the total number, accomplished natural spontaneous delivery; the lowest incidence of operative delivery, 16.2 per

cent, was in the antepartum group (Table VII). The chief indication for operative vaginal delivery was prolongation of the second stage of labor, with possible jeopardy to both mother and child.

TABLE VII. METHOD OF DELIVERY

	TYPE OF ECLAMPSIA			PER CENT OF TOTAL CASES
	NUMBER OF CASES			
	ANTEPARTUM	INTRAPARTUM	POSTPARTUM	
Vaginal Delivery	71	25	37	93.7
Spontaneous	62	18	29	76.8
Forceps	5	4	6	
Breech extraction	2	2	1	
Version and extraction	1		1	
Embryotomy	1	1		
Abdominal Delivery	3	5	1	6.3
Cesarean section	3	3	1	
Cesarean section plus hysterectomy		2		
Total	74	30	38	100.0

Cesarean section was performed only nine times, 6.3 per cent, and eclampsia per se was the indication for section in only four of these patients. Dystocia furnished the indication in two cases, and placenta previa, abruptio placentae, and infection plus dystocia in one case each. Cesarean section was followed by hysterectomy in the last two cases mentioned. Abdominal delivery was performed only once in the 51 cases handled in the last two years, in the patient who required the Porro operation for infection and dystocia, and the declining incidence of section is an interesting commentary on our increasing tendency to treat the disease rather than the pregnancy.

Local analgesia was used for all varieties of operative work. We consider all other forms of anesthesia dangerous in eclampsia, and have made no exception of caudal techniques since we observed a patient with pre-eclampsia develop convulsions five hours after delivery under continuous caudal analgesia.

Although labor is short and delivery easy in most cases of eclampsia, constant watchfulness must be maintained, for the ordinary hazards of parturition are always increased. Irritation and trauma, whether endogenous or exogenous, may precipitate convulsions and make control increasingly difficult. Restlessness may make sedation necessary. The low urinary output frequently encountered late in labor may call for special therapeutic measures. The abrupt development of such complications as pulmonary edema and vascular collapse may tax one's ingenuity to the uttermost.

Obstetric complications, furthermore, are not uncommon, and their management is difficult because these patients do not tolerate even ordinary manipulations and ordinary blood loss. It is not always easy to determine whether the conditions encountered are due to eclampsia, to normal or abnormal circumstances of parturition, to the therapeutic

measures adopted for the control of eclampsia, or to the cumulative effect of all these factors. Eclampsia is the basic disease, it is true, but the obstetric complications cannot be disregarded.

The complications which occurred in this series involved 21 per cent of the patients. They included hemorrhagic complications in 13 cases (abruptio placentae in 7 cases, postpartum hemorrhage in 4, and placenta previa in 2), vascular collapse in 3 cases, polyhydramnios, serious dystocia and severe intrapartum infection in 2 cases each. Eight cases had severe anemia.

The Management of the Puerperium

The rather general belief that the successful termination of labor is equivalent to the successful termination of the eclamptic state is by no means justified. It is true that in no case in our series did convulsions recur after delivery, and that in most instances definite amelioration of toxic manifestations occurred within 24 hours of delivery; even cases of intercurrent eclampsia usually responded with increased diuresis during this period. On the other hand, in the 104 cases of antepartum and intrapartum eclampsia in this series, there were at this time three instances of peripheral vascular collapse, and four instances each of postpartum hemorrhage, persistent anuria, and profound coma.

Convulsions and serious complications not infrequently develop following delivery, certain precautions, in addition to routine postpartum measures, are necessary during the puerperium and, in particular, immediately after delivery. An intravenous infusion of 20 per cent dextrose solution in the amount of 500 c.c. is begun as soon as the patient is prepared for delivery, and is administered very slowly. This measure aids in the prevention of shock and collapse when the child is born, and obviates the difficulty of entrance into veins if vascular collapse should occur. Morphine is administered as soon as delivery is completed.

The blood pressure and urinary output are checked regularly throughout the period of hospitalization, and mother and child are kept in the hospital for a minimum of 10 days and preferably for 14 days. Although 50 per cent of postpartum convulsions occur within 8 hours of delivery, they can begin much later (41 hours in this series), and prolonged observation of potentially eclamptic patients is imperative.

The patient then returns at regular intervals to the postpartum clinic, and it is impressed upon her that she should submit herself to examination at regular intervals throughout the remainder of her life, especially if she again becomes pregnant.

Results of Therapy

Maternal Results.—The fact that there were no maternal deaths in these 142 cases of eclampsia, we attribute to our strict adherence to

the plan of treatment just outlined. On the other hand, we were not asked in this series to accomplish the impossible. Patients transported from distant areas did not succumb before treatment could be administered, and we encountered no cases of such uncommon but apparently invariably fatal complications as acute heart failure, extensive cerebral hemorrhage, or massive pulmonary edema of degrees incompatible with life.

From the standpoint of morbidity, we were less successful, for, by accepted standards, it averaged 36.6 per cent, which is more than four times greater than the incidence in our usual obstetric census. The rate was highest in the postpartum group (57.8 per cent) and lower by 40 per cent (22.9 per cent) in the antepartum group, most of the patients in which had recovered from the acute phase of the disease. It was 43.3 per cent in the intrapartum group. Hyperpyrexia, with temperatures above 104° F. during the convulsive or comatose stages, occurred in four cases, probably as the result of temporary derangement of the temperature centers by vasospasm or edema. Other common extragenital causes of fever were pulmonary congestion and edema, urinary tract infections, and reactions to parenteral fluids or to sedation.

Seventy-eight per cent (26) of the 33 patients delivered by operative means had febrile puerperia, and this increased susceptibility should serve as a warning to limit intervention in eclampsia to cases in which the indications are indubitable.

Fetal Results.—Of the 149 children born to the 142 mothers in this series, 113, 75.8 per cent, were discharged from the hospital in satisfactory condition. Although the fetal case fatality was 24.2 per cent (36), the salvage from the seven twin pregnancies fortunately permitted 111 women to leave the hospital with children.

Previability and prematurity were responsible for 31 of the 36 fetal deaths (86.1 per cent). Among the 5 mature infants who failed to survive, premature separation of the placenta was the cause of 1 death and intrapartum uterine infection of another, but in the other 3 cases no definite cause was found. Twenty-two babies were stillborn, several of whom were dead when the mother was admitted to the hospital. Necropsies were done in 25 cases, in 16 of which (64 per cent) varying degrees of intracranial hemorrhage were found.

Birth weights (Table VIII), which were invariably less than the clinic average for similar stages of pregnancy, showed the direct effect of toxemia upon the fetal growth and development, as well as the effect of prematurity. Fourteen babies (10 per cent) weighed less than 1,500 Gm., and were classed as previable; 62 others (42 per cent) weighed between 1,500 and 2,500 Gm., and were classed as premature. Most of the remaining 73 children, despite the increased gestation period and increased birth weight, appeared toxic and immature. The proportion of survivors, however, almost consistently increased in direct ratio to increases in the birth weights.

Twenty-four of the 36 deaths occurred in the antepartum group (32.4 per cent), 8 in the intrapartum group (26.6 per cent), and 4 in the postpartum group (10.5 per cent). The lowest fetal case fatality would naturally be expected in the group which escapes the shock of convulsions and is least affected by prematurity, and the highest would be expected in the group affected by the combination of prematurity and convulsions. The fetal mortality in severe eclampsia was 36 per cent, as compared with 23 per cent in mild eclampsia.

TABLE VIII. FETAL DEATHS IN RELATION TO FETAL BIRTH WEIGHTS

BIRTH WEIGHT	TOTAL CASES	DIED		SURVIVED	
		STILLBORN	NEONATAL	NUMBER	PER CENT
Under 1,000 Gm.	4	3	1		
1,000 to 1,499 Gm.	10	5	3	2	20.0
1,500 to 1,999 Gm.	25	8	5	12	48.0
2,000 to 2,499 Gm.	37	3	3	31	83.8
2,500 to 3,499 Gm.	65	3	1	61	93.8
3,500 Gm. and over	8		1	7	87.5
Total	149	22	14	113	75.8

Incidence of mortality—24.2 per cent

Average weight of all babies----------2,660 Gm.
26% of all babies weighed less than----------2,000 Gm.
67% of all dead babies weighed less than------2,000 Gm.
64% of all babies under 2,000 Gm., died.

Although the fetal case fatality in this series compares favorably with that in other reports in the literature, in retrospect we consider it unnecessarily high. In the early years of this study we believed a high fetal mortality inevitable in eclampsia, and we hesitated to do anything for the sake of an infant whose existence seemed precarious at best, lest we jeopardize the mother's safety. In later years, we have found that resonable attention to the baby yields high dividends. We have not changed our basic plan of treatment in any way for the child's sake, but in the last two years of this study, with the close cooperation of the Department of Pediatrics, we have achieved a gross fetal mortality of 17.6 per cent in 51 cases. Undoubtedly, this rate can be still further improved by proper attention to the child before, during, and after delivery.

Follow-Up

Seventy-two patients, more than 50 per cent, were normal in all respects on their discharge from the hospital from 5 to 31 days after delivery, and it is significant that no woman in this group later exhibited hypertension. In two instances, complete amaurosis had returned to normal by this time.

The remaining 70 patients presented blood pressure elevations of 140/90 or higher when they were dismissed from the hospital after delivery, and 11 of these presented associated albuminuria. It is significant that the elevations of blood pressure occurred in only 36 per cent (9) of the 25 patients with intercurrent eclampsia of more than seven days' duration, as compared with 32 of the 49 patients who had been delivered within 7 days after their seizures (65 per cent), and 41 of the 74 patients who comprised the whole group of patients with antepartum eclampsia (55 per cent).

Elevated pressures were also observed in 19 of the 30 patients with intrapartum eclampsia (63 per cent) and in 10 of the 38 patients with postpartum eclampsia (26 per cent).

Eighty-five of the 142 patients were observed in the clinic at periods varying from 5 to 12 weeks after delivery. Seventy-three were then normal in all respects (42 of 49 in the antepartum group, 15 of 18 in the intrapartum group, 16 of 18 of the postpartum group). The re-

maining patients had elevations of blood pressure above 140/90. Again it is significant that only 2 of the 18 patients in the intercurrent group presented elevated pressures, as compared with 5 of the 31 patients in the antepartum group who had been delivered within 7 days.

Forty-six of the 142 patients were again observed at periods varying from 1 to five years after their attacks of eclampsia. All these patients were admitted to the hospital, where investigation included complete physical examination, urinalysis, blood chemical determinations, urea clearance tests, tests of hepatic function, electrocardiographic studies, and studies of vasomotor lability. The only abnormalities apparent in any of these tests were persistently elevated blood pressures, varying from 140/90 to 170/110, in 3 patients, who were regarded as having hypertensive vascular disease. Again, it seems significant that only one of the 11 patients re-examined in the intercurrent group exhibited this abnormality, as compared with 1 of the 15 re-examined in the group delivered within 7 days of their seizure, and 1 of the 12 re-examined in the intrapartum group. No elevated pressures were observed in the 8 patients with postpartum eclampsia who were re-examined.

The number of patients re-examined is small and the period of observation somewhat limited, but the results to date do not suggest that eclampsia, regardless of its type, severity or duration, causes permanent vascular or renal damage or any other sequelae.

Thirty-four of the 142 patients have been followed in 56 subsequent pregnancies. Eleven women had 2 pregnancies each, 4 had 3 pregnancies each, and 1 had 4 pregnancies within the five-year period of observation. Forty-six of these pregnancies in 26 patients (76.4 per cent of the group followed-up) were normal in all respects, including the 4 pregnancies in the five-year period.

The remaining 8 patients, however, who went through 10 subsequent pregnancies, all exhibited some form of toxemia at some time. One patient had a recurrence of eclampsia, the conditions in both pregnancies being identical: After more than average prenatal care, mild pre-eclampsia developed and culminated abruptly in convulsions during labor. One patient developed mild pre-eclampsia in the first subsequent pregnancy and severe pre-eclampsia in the second, the blood pressure and urine being normal in the interims. It would seem advisable to terminate childbearing in both these women, as well as in 2 other women who were found to have persistent hypertension in the second and the third pregnancy, respectively, after the pregnancies in which eclampsia developed. Three other women had mild pre-eclampsia in one successive pregnancy each, and the remaining patient had the same condition in two successive pregnancies; it would seem best either to sterilize this latter patient, or to advise the use of contraceptive measures until her true status can be determined.

Although the incidence of toxemia in the posteclamptic group is approximately double the clinic average, it is doubtful whether eclampsia should be regarded as the only cause of the increase. If comparison were made with a group of women subjected to the similar stress and strain of repeated pregnancies in rapid succession, but without a history of eclampsia, the incidence would probably be much the same. On the other hand, the high rate of fecundity warrants consideration, for it undoubtedly accelerates, or at least aggravates, the development of potential, incipient, or active vascular or renal disease. Eclampsia

by no means precludes the possibility of subsequent normal pregnancy, but childspacing is advisable, and medical care in subsequent pregnancies is imperative.

Prophylaxis

Reports in the literature are unanimous in emphasizing the value of prenatal care in the prophylaxis of eclampsia, and the lack of such care was the obvious cause of the development of most cases in this series (Table IX). In 91 cases, almost 65 per cent of the total, the patients had no care of any kind during their pregnancies, and in another 37 cases such care as they had was entirely inadequate by modern obstetric standards.

It might be interpolated here that the financial status and intelligence ratings of these women compared favorably with the general average in such material.

Eclampsia developed in only 14 patients who attended the clinic regularly throughout pregnancy, and at first glance all of them seemed to have received excellent prenatal care. Closer investigation, however, usually revealed lack of full cooperation on their part, or errors of judgment on the part of the physician, in sharp contrast to modern concepts of adequate and intelligent prenatal supervision. Curiously, defections, most of which occurred late in pregnancy, were explained in the same way in almost all cases; the patients were "too sick to come to clinic" or "too sick to do what the doctor said."

Even under the best of circumstances eclampsia is not entirely preventable. Occasionally, a rapidly fulminating pre-eclamptic toxemia culminates in convulsions without the usual, gradually progressive phases, and still more occasionally all antecedent manifestations are absent. Three of our cases were in the latter category. The patients were apparently normal in all respects throughout their pregnancies, and had received competent medical attention in the prenatal clinic, 6, 14 and 21 hours, respectively, prior to the onset of convulsions. One patient complained of a mild antecendent headache, but in the other two cases, so far as could be determined, there were no premonitory symptoms or signs of any sort.

TABLE IX. PREVENTION AND RESPONSIBILITY IN RELATION TO THE TYPES OF ECLAMPSIA

TYPE OF ECLAMPSIA	PRENATAL CARE			ONSET OF CONVULSIONS		
	ADEQUATE	INADEQUATE	NONE	AT HOME	IN HOSPITAL	EN ROUTE TO HOSPITAL
Antepartum	8	20	46	47	15	12
Intrapartum	4	12	14	11	16	3
Postpartum	2	5	31	10	26	2
Total	14	37	91	68	57	17
Per cent	9.9	26	64.1	48	40.1	11.9

NOTE: A detailed case report is appended, which may clarify the plan of management in a typical case.

RÉSUMÉ OF CLINICAL COURSE AND TREATMENT IN A TYPICAL CASE (HOSPITAL NO. L-42-69985) OF ANTEPARTUM ECLAMPSIA IN AN 18-YEAR-OLD COLORED NULLIPARA WHO HAD NO PRENATAL CARE

DATE	BLOOD PRESSURE	URINE		EDEMA	BLOOD CHEMISTRY	CLINICAL CONDITION	TREATMENT
		C.C.	ALBUMIN				
11/9/42							
2:45 P.M.	190/120			+++	Hematocrit* 55.0 Uric acid† 6.9 Serum protein† 5.8	5 convulsions before admission, 1 on admission	2:45 P.M. Morphine sulfate, ¼ gr. } subcutaneously Sodium phenobarbital, 5 gr. }
3:00 P.M.	170/110	20 (casts)	Boiled solid	Lungs −+ Face ++			3:00 P.M. Retention catheter
3:30 P.M.	175/110					Restless, spastic	3:30 P.M. Magnesium sulfate (10%) 20 c.c. intravenously
4:00 P.M.	180/110	12					4:05 P.M. Nasal oxygen Glucose (20%) 500 c.c. intravenously
6:00 P.M.	160/110	25				Semicomatose	6:00 P.M. Phenobarbital, 5 gr. subcutaneously
8:00 P.M.	160/115	65	++++			Irrational	
10:00 P.M.	165/115	15			Hematocrit 50.0	Vomiting	10:00 P.M. Glucose (10%) 1,000 c.c. intravenously
12:00 M.	160/100	185	+++	++++		T. 103.2 F.; P. 120; R. 40	12:00 M. Magnesium sulfate (10%) 20 c.c. intravenously
11/10/42							
2:15 A.M.	180/112					Semicomatose Stuporous, irritable	2:15 A.M. Glucose (50%) 50 c.c. intravenously
3:30 A.M.	162/105	455					3:30 A.M. Phenobarbital, 5 gr. subcutaneously
8:00 A.M.	170/120	280	+++	+++		Restless Conscious, drowsy	8:00 A.M. Phenobarbital, 5 gr. subcutaneously
12:00 M.	160/100	20			Hematocrit 42.0 Uric acid 4.9 Serum protein 5.2	Retinal vasospasm and edema	12:00 M. Glucose (20%) 500 c.c. intravenously Force fluids orally
4:30 P.M.	155/110	300					4:30 P.M. Magnesium sulfate orally
8:00 P.M.	175/115	590	++	++		Headache	8:00 P.M. Enema
12:00 N.	145/100	725				T. 99 F.; P. 100; R. 22	24-hour fluid intake—3,780 c.c.

*In cell volume per cent.
†In mg. per cent.
‡In Gm. per cent.

11/11/42 8:00 A.M. 4:00 P.M. 12:00 M.	140/100 148/105 155/105	No casts 4485	++ + +	++ Lungs—negative	Hematocrit 36.0 Serum protein 5.7	Rational Sleeping, quiet T. 97.8; P. 84; R. 20	Diet: protein 100 Gm., salt free Fluids: forced to 5,000 c.c. orally Sedation: phenobarbital orally, P.R.N. Elimination: magnesium sulfate orally Intake—5,100 c.c.
11/12/42	155/115	3535	0	+		Mild headache	Intake—3,950 c.c.
11/13/42	144/100	4260	+	+		Cooperative	Intake—5,700 c.c.
11/15/42	150/110	4900	++	Ankles	Hematocrit 36.1	No complaints	Medical induction Intake—4,080 c.c.
11/18/42	140/90	3690	0	0		No complaints	Medical induction Intake—4,330 c.c.
11/20/42	150/90	3745	0	0			Medical induction, membranes stripped
11/21/42 A.M. P.M.	 168/100 140/100	 920 485	 + +	 0 0		Labor—13 hours Baby—alive; wt. 6.1 pounds	Labor: Morphine, gr. ¼; glucose (20%) 500 c.c. Delivery: low forceps, episiotomy; local analgesia. Morphine and glucose infusion during delivery
11/22/42	140/90	3160	Tr.	0			
11/29/42	135/85		0	0	Hemoglobin‡ 10.0 Hematocrit 32.5 Serum protein 6.2	Mother and baby in good condition	Discharged from hospital
1/ 6/43	120/80	Sediment negative	0	0		Same	
12/14/43	108/65	Sediment negative	0	0	Hemoglobin 11.1 Uric acid 3.8 Serum protein 7.5	Mother and baby in excellent condition	Electrocardiogram—negative Ocular fundi—negative
3/22/44	110/78						Electroencephalogram—normal

Seventeen patients had their first seizures while en route to the hospital (Table IX) and 57 others after being admitted to the hospital. Most of these women sought aid because of fulminating symptoms, such as severe headache, drowsiness, dim vision, vomiting, or marked edema, but 5 other patients came merely because they "felt funny" and evidently had premonitions of danger.

A review of the cases in which the first convulsions occurred after hospitalization shows that in at least 34, adequate attention, sufficient sedation, the use of hypertonic dextrose solution, and the induction of labor might have prevented the convulsions. These cases all represent failures of management, though the human factor could not always be held responsible. In the remaining 23 cases, the seizures occurred within two hours of hospitalization and could scarcely have been prevented.

These 142 cases bear witness to another precaution quite as important as prenatal care but less often emphasized, namely, that intelligent care and good judgment are as essential during labor and after delivery as during the antenatal period. In this series 68 patients, 47.9 per cent, had intrapartum or postpartum convulsions, and it is reasonable to speculate that if parturition and the early puerperium had been managed with more attention to possible dangers, some if not all of these seizures might have been prevented.

Summary and Conclusions

1. There is presented in this paper a plan of management of eclampsia as the result of which no maternal deaths occurred in 142 personally supervised cases. So far as can be determined, this is the largest successful series to be recorded.

2. The therapeutic regimen outlined is neither new nor original, but it is believed that the details of its application are not always carried out with the care with which they were applied in this series. To that unremitting care are attributed the successes which were achieved.

3. The plan is based on (a) an ultraconservative concept of management, in which the dangers of both overtreatment and indiscriminate treatment are evaluated; (b) constant (in the most literal sense of the word) observation of each eclamptic patient by an experienced staff throughout the entire course of treatment, which permits (c) careful integration of the various therapeutic components into an individualized regimen rather than their application as a standard routine of treatment.

4. Special factors of success also include: (a) frequent changes of posture, plus the use of oxygen therapy and of aspiration, during the acute phases of the disease; (b) limitation of sedation to the dosage necessary to control convulsions and hyperirritability; (c) limitation of dextrose therapy to the smallest amount necessary to insure a satisfactory urinary output, with a return to oral fluids in maximum amount as soon as the swallowing reflex returns; (d) delaying labor

(unless it ensues spontaneously) until the optimum recovery from the acute stage has taken place; (e) induction of labor at the optimum time and by the simplest possible method, medical induction being repeated if the first attempts are not successful; (f) limitation of operative intervention to the irreducible minimum, and the use of local analgesia for all forms of operative work.

5. Neither the patients' future health nor their subsequent pregnancies are in any way jeopardized by this plan of management. This statement is based upon (a) observation of 85 patients at intervals of from 5 to 12 weeks after delivery; (b) of 46 patients at intervals of from 1 to 5 years after delivery; (c) and of 34 patients in 56 subsequent pregnancies. The incidence of residua was no larger in the intercurrent group of patients than in the whole group followed up and was smaller than in some of the subgroups.

6. Adequate consideration of the baby yields high dividends in fetal salvage without increasing the maternal risk. The fetal case fatality in this series was 24.2 per cent; it showed marked improvement in the last two years, when the principle of consideration for the child was increasingly applied.

7. Lack of adequate prophylaxis was the factor chiefly responsible for the development of eclampsia in these 142 cases. In this respect, adequate care during gestation is not sufficient. Intelligent care and sound judgment are also needed during labor, at delivery, and throughout the puerperium.

Discussion in the Papers by Drs. Huber and Arnell

DR. CHARLES H. PECKHAM, Cooperstown, N. Y.—Dr. Arnell is to be congratulated on such a lengthy series of cases without a maternal death, but I am afraid my own experience more closely parallels that of Dr. Huber.

Since the incidences of and mortality from eclampsia apparently vary greatly in different localities of this country, as well as in different parts of the world, attempts to adduce conclusions from comparative statistics are open to a good deal of criticism. The transition from so-called radical to conservative therapy began about thirty years ago, and the latter has been the rule in most clinics in this country for about twenty years. Conservative regimes of treatment at present differ essentially only in the type of sedative drugs employed. Morphine, magnesium sulfate, sodium luminal, sodium amytal, chloral hydrate and paraldehyde have probably been employed most frequently. Since the main object of drug therapy is the prompt control of the convulsive seizures, it is interesting to speculate why one drug works better for one clinician and a different one for another. The answer is probably very simple—none is completely satisfactory.

It is a matter of rather general agreement that present therapy gives satisfactory results in cases of eclampsia classified as mild, but leaves a great deal to be desired in the severe type. A number of years ago, I analyzed the records of 152 cases of convulsive toxemia of pregnancy divided into mild and severe groups according to a proposed modified Eden type of classification. No maternal deaths occurred in 71 cases denoted as mild, while in 81 instances of severe eclampsia the mortality was 18.5 per cent. It was also noted that as conservative treatment replaced radical, the mortality from antepartum eclampsia fell to one-half of that formerly observed, intrapartum to one-quarter, while the results in

the postpartum type were unchanged. As a matter of fact, postpartum eclampsia in my experience as opposed to that of many others, carries a higher mortality rate than that of the other types.

The death rate from eclampsia has furthermore shown a general tendency to decline during the past ten years. Is this due to improved treatment or a decline in severity of the disease? Some time ago an article appeared in the literature demonstrating a lower mortality from eclampsia coincident with certain alterations in therapeusis; during the same time interval, a similar decrease was noted at the Johns Hopkins Hospital although therapy was unchanged. Most authorities attest to a lowered incidence of eclampsia itself. Is this due to a generally improved prenatal regime, to better treatment of the patient with early toxemia, or to an increased tendency to terminate the pregnancy immediately if severe pre-eclampsia manifests itself? All of these three probably play a role, but the prophylactic emptying of the uterus by whatever means seems best has not yet received the popularity it deserves.

Dr. Arnell's remarks concerning the treatment of the early toxemic patient cannot be too strongly emphasized. The importance of proper elimination and the prohibition of salt in the diet is generally agreed upon. On the other hand, we have only begun to realize the importance of the protein problem. Fifteen years ago patients with toxemia of pregnancy were placed upon low protein diets and seemed to improve. Why? One wonders if the type of protein previously ingested supplies at least a partial answer. The diet of the average ward patient is frequently deficient in milk, eggs, and cheese, and the principal source of protein is often ham and pork. Gastroenterologists agree that pork and veal are by far the most difficult meats to be assimilated by digestive processes. If it is agreed that the toxemic patient requires in the neighborhood of 100 grams of protein per day, these can safely be supplied by a quart of milk, two eggs, the usual fruits and vegetables, one serving of cheese and one of meat.

I question the wisdom of allowing the patient with a live fetus to proceed indefinitely with her pregnancy subsequent to the convulsive episode. The post-eclamptic pre-eclamptic is not a good risk. Besides the possibility of a second attack of convulsions, there is a real danger to the fetus in utero and, in my opinion, an increased probability of the patient being left with permanent vascular damage. In this regard it seems appropriate to state that in other follow-up studies the incidence of vascular damage has been much higher than is the case in Dr. Arnell's series.

DR. FREDERICK H. FALLS, Chicago, Ill.—The paper of Dr. Huber clearly indicates the disastrous effects of delay in starting the management of eclamptogenic toxemia. Adequate prenatal care would have eliminated most of the cases from the convulsive group. As long as this type of case continues to be dumped in on the attending staff of clinics, just as long will these patients fail to make recoveries. The situation is analogous to what occurred in typhoid fever in the days before the pathology of this disease was understood. Patients were allowed to eat whatever they wished and a certain percentage of them developed a perforated typhoid ulcer. Those who had this serious complication very frequently died because they were untreated until the rupture occurred, and then all the surgical skill in the world was of little avail.

The patients with eclamptogenic toxemia that is permitted to go to the convulsive stage of the disease is the victim of neglect. She or her physician may be responsible for the neglect, and the responsibility may be great or small depending on whether the toxemia was slowly developing or fulminating in its onset. The solution lies, therefore, as was suggested in the paper, in furnishing sufficient prenatal care to detect the advent of serious symptoms before the convulsive stage arises. This can be done in all but a very small percentage of

cases (the fulminating variety). We are pessimistic about the medical management of these cases from the start, and we do not temporize. If the baby is alive, the uterus is opened from above just as rapidly as we can provide proper facilities for operating. If the baby is dead, we do not operate since we feel that the cause of the disease is removed (leakage of toxins from placenta) and that medical management will handle the toxemia satisfactorily. Thus, we avoid, if possible, all very real dangers of operating on these toxemic women. Dr. Huber's suggestions would be more convincing if he had done cesarean sections on some of these cases.

I have done cesarean section in 49 cases of eclampetogenic toxemia which were of the fulminating type or which had failed to respond to medical management and were, therefore, developing into severe toxemias. There were no deaths in this series. Thirteen of these patients had convulsions either during, before or after delivery. These are part of my series of 1,200 eclamptogenic toxemias in which I had a mortality of 0.6 per cent for the mothers and a gross fetal mortality of 11.9 per cent.

These patients were all clinic cases in a teaching hospital. All were handled by the resident staff according to a simple management including bed rest, saline catharsis, milk diet, and, in relatively few cases, glucose and magnesium sulfate parenterally. I am not convinced of the desirability of large doses of hypertonic glucose, and I am definitely opposed to blood transfusion in eclamptics unless absolutely necessitated by severe anemia. I think anyone who has taken the trouble to study the coagulability of the blood in eclamptics will agree that the hazards of fluid transfusion are greatly enhanced. I do not think that the Rh factor can explain all of these untoward reactions, although it may be responsible for some.

The incidence of symptoms of cerebral hemorrhage in 6 cases is worthy of note. This complication is hardly mentioned in most of the literature. However, Dr. Jaffé stated that at autopsy in eclamptics he found this frequently as the cause of death. There are not enough complete postmortem examinations being done on women dying of eclampsia, to complete our knowledge on this subject.

Dr. Arnell's paper stresses the importance of conservative medical management also, but I am in some doubt about his figures. He states that during the five-year period, 162 women with convulsions were admitted to the obstetrical service but that only 120 of them were eclamptics. However, he bases his statistics on a group of 142 cases of eclampsia. I should like to ask if there were any deaths in the 42 cases classified as not eclamptics, and if so was an autopsy performed, and if so what were the findings.

According to our experience, the eye ground findings in toxemias of pregnancy are of comparatively little diagnostic or prognostic value in the immediate handling of a given case. We have repeatedly put the eye consultant on the spot, so to speak, and he has not been able to contribute much to the management of the case.

On the other hand, I am convinced that the kidney function test which Dr. Arnell thinks of little or no value is of considerable value in the preconvulsive stage of eclamptogenic toxemia, and I think that it would be of value in managing the postconvulsive stage that he describes, preceding the onset of labor.

Spinal drainage, as recommended by Koenig many years ago, has been tried and given up. Its use is dangerous because of the possibility of sudden death from herniation of the brain down through the foramen magnum when the pressure is reduced from below. An additional danger is the breaking off of a spinal needle if the patient has a convulsion while the needle is being inserted or is in place.

Nasal oxygen has a real place in those cases showing marked pulmonary edema. Lowering the head to promote pulmonary drainage is open to question, since it increases intracerebral pressure.

Contrary to the experience of Dr. Arnell, we have found venesection an extremely valuable procedure in eclamptic convulsions, and only contraindicated in patients with a definite anemia. If we are to operate, we usually postpone the venesection until we know what the operative blood loss is, and then supplement it if necessary. We aim at the removal of about 500 c.c., since lesser amounts are usually of little avail.

This is a remarkable series of cases of convulsive toxemia without a death and in spite of my leaning toward radical treatment of the fulminating case leaves me in doubt as to its necessity if such results can be obtained by a more conservative management.

DR. KARL M. WILSON, Rochester, N. Y.—I would like to ask the authors whether they have any observations on the plasma protein in their severe toxemia cases? In some of these, the plasma proteins of course may be well below the edema level. When that is the case, the seriousness of the situation is of course aggravated, but at the same time I have been quite impressed with the results obtained by building up the plasma protein level. This can be done in three ways: (a) By the administration of protein food by mouth if the patient can take it, but this will be slow; (b) more rapidly by the administration of amino acids and the subsequent building up of plasma protein in the circulation; and (c) most rapid of all by the administration of plasma transfusion.

DR. FRED L. ADAIR, Chicago, Ill.—Certain critical responsibilities have been shown by both Dr. Huber and Dr. Arnell in connection with their presentations. They both agree, I think, that primary eclampsia is lessened greatly by adequate attention during pregnancy. This has been inadequate in their series, as in other series, and I think the medical profession and the laity as a whole, are negligent in procuring this adequate care.

They both agree, as I believe, that not all types of eclampsia can be placed in the same category, that attacks differ a great deal in their severity. It has always been difficult to say what treatment is radical or conservative as these terms have no uniform meaning. I think anything that saves life or health is conservative. Consequently, in certain cases surgical treatment may be conservative and medical treatment may be radical. Both series indicate that there are certain cases so severe—and I think Dr. Falls also referred to this and agrees with this point—that they do not respond to medical treatment, and consequently, prompt emptying of the uterus is indicated in intelligently selected cases. Now this may be accomplished from below or above, but I think we have to be extremely careful in advocating such operative procedures as cesarean section in eclampsia. While in clinics under expert observation, it may be quite possible to select cases which will respond more satisfactorily to delivery by cesarean section, if such therapy should become widespread the results would be disastrous to many patients.

An important consideration is the time when these cases should be operated upon. A patient in a convulsive or comatose state is a poor surgical risk. If we can carry such a case into a phase where all the functions of the patient are less seriously disordered, it is a much safer time to do cesarean section.

There are several other points in Dr. Arnell's paper which are extremely important. First, the care of the patient should not be delegated to obstetrically inexperienced personnel as interns and nurses. Second, the care of the eclamptic patient should be continuous until the patient is safely beyond any acute episode such as a convulsion or coma. Furthermore, it seems obvious that inasmuch as

we are treating individuals and a condition which is subject to a great deal of variation, that the treatment must be individualized. This can be done best by some one who has had considerable experience in the treatment of this condition, namely, a well-trained, experienced and competent obstetrician.

DR. THADDEUS L. MONTGOMERY, Philadelphia, Pa.—To any one who sees a large volume of obstetric material, it is obvious that not all cases of fully developed eclampsia can be saved. Although Dr. Huber has had discouraging results with his smaller series of cases, and Dr. Arnell astonishingly good results with a larger one, the differences between these groups will probably grow less perceptible as time goes on, for a certain number of patients admitted in extremis will die, and a certain percentage will inevitably succumb to cerebral hemorrhage in any man's clinic.

However, I am of the opinion that conservative medical treatment is still the thing in eclampsia. I would hate to see a reversion to hasty surgery in these terribly ill, poor risk subjects. I wish only that Dr. Arnell had given us a more complete description of his successful therapeutic methods.

There are certain fundamental principles to be observed in the medical management of this disease which cannot be departed from too far. Convulsions must be controlled, the patient must be put at rest, edema of vital tissues must be eliminated, organs of elimination must be stimulated and not suppressed, respiration and oxygen transportation must be encouraged.

Since following Professor Jesse O. Arnold at the Temple University, I have had the privilege of observing first hand the results of a dehydration therapy which he and Temple Fay developed at that institution. With few modifications (notably the addition of protein to dietary intake) we have followed their procedure. You may remember that the method calls for only enough morphine to gain preliminary control of the patient. Dehydration, and incidentally further sedation, is achieved by spinal puncture, intravenous hypertonic solutions, and active purgation. The objection to spinal puncture in these cases has appeared more academic than practical. Oxygen is administered freely. Particularly avoided are the barbiturates and their depressing effect upon respiration and oxygen exchange.

Of course, eclampsia itself is a rather rare disease in the larger northern cities, and we have had comparatively few cases in the past four years. However, in these I have been most favorably impressed with the treatment described.

DR. HUBER (closing).—Replying to Dr. Wilson's question concerning the plasma proteins, we have routinely made determinations upon our patients with toxemia of pregnancy and in general the level has been on the low side of normal. There did not seem to be a significant difference in the level in patients with severe or mild eclampsia.

I am very glad that Dr. Adair pointed out that there are great variations in what may be termed severe eclampsia. I am convinced that in this series, the group represented a degree of severity that is out of proportion to that which is usually classified as severe. Most of these patients are to be looked upon as patients who were neglected cases of severe eclampsia and our problem was primarily that of salvaging as many mothers and infants as possible where the prognosis was already very poor. It was from that point of view that the paper was presented.

DR. ARNELL (closing).—Replying to Dr. Falls' question regarding the source of the material requires the explanation that eclamptic admissions to two hospitals were under our management. The series embraces 142 consecutive cases and includes all cases of eclampsia admitted to our services during the period

under consideration. Convulsions due to causes other than toxemia were mentioned to emphasize the point that pregnancy with convulsions does not always mean eclampsia.

Neither blood transfusion nor spinal drainage is a routine procedure in our treatment of eclampsia. However, we have found transfusion of value in treating some cases of persistent anuria as well as in combating vascular collapse and hemorrhage. In our experience, spinal drainage often has a beneficial effect on the infrequent case showing an unusual degree of cerebral irritation.

In answer to Dr. Wilson's question regarding serum protein levels, we found the average concentration definitely lower than normal, with the greatest decrease in the albumin fraction.

THE FAILURE OF THE CONSERVATIVE TREATMENT OF ECLAMPSIA*

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ECLAMPSIA is justifiably considered preventable. Its development usually indicates the failure of the patient to obtain adequate prenatal care or the failure of the physician to recognize the severity of the developing toxemia.

All patients with eclampsia do not have the same serious prognosis. The patient who develops her initial convulsion during the course of labor has, in general, a better prognosis than the patient with antepartum convulsions. The postpartum eclamptic, unless neglected, has a still better prognosis. There is, in fact, a great variation in the severity of eclampsia developing before the onset of labor so that some patients are easily controlled while others progress to a fatal termination in spite of any therapy that may be undertaken.

During the five-year period from January 1, 1938 to December 31, 1943, there were 6,994 patients delivered in the William H. Coleman Hospital, Indiana University Medical Center. There were 51 eclamptic patients during this time. This represents a gross incidence of 7 in each 1,000 deliveries. Thirty-seven of the 51 eclamptic patients were admitted to the hospital as emergencies and had not been previously seen by our staff. We accept responsibility for the development of eclampsia in the remaining 14 patients, an incidence of 2 in each 1,000 deliveries.

It is perhaps interesting to note that eclampsia appeared in our service during every month of the year but January. Thirty-six per cent of the eclamptic patients, however, were seen during the months of May and June. Only 9 of the 51 patients had had more than one previous delivery and 35 were pregnant for the first time. Eighty-four per cent were under 30 years of age.

In the total series there were 12 maternal deaths, a loss of 23.5 per cent. There were also 18 fetal and neonatal deaths, an infant mortality of 35 per cent. These results are so poor that further analysis of them is imperative.

The 14 patients who developed eclampsia after receiving prenatal care in our clinic or in the private practice of our staff formed a distinct group. Eight of them developed their initial convulsion post partum and none had more than 3 convulsions. Thirteen infants survived. The one fetal death was a stillborn premature infant delivered at 30 weeks, 12 days following the only convulsion the patient experienced. One maternal death occurred in this group.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

This patient was a 21-year-old primigravida, 6 weeks from term, who had been under hospital observation and treatment for 18 days with apparent improvement. She suddenly developed severe epigastric pain and headache and while preparations were being made for cesarean delivery, she had a single eclamptic convulsion. A living premature infant was delivered. The patient failed to respond to therapy and died eight hours after the operation.

In comparison the remaining 37 patients formed a definitely different group. They were all emergency admissions and had developed eclampsia before the onset of labor. Using the criteria suggested by Dieckmann,[1] 13 of this group were classified as having severe eclampsia. This included patients who showed one or more of the following conditions:

1. Coma.
2. Temperature of 102° F. or more.
3. Pulse rate over 120.
4. Respiratory rate over 35.
5. More than 10 convulsions.
6. Cardiovascular impairment (edema of the lungs, persistent cyanosis, low or falling blood pressure, low pulse pressure, etc.).
7. Failure of treatment to:
   (a) Stop the convulsions or prevent their recurrence.
   (b) Produce a urinary output of at least 700 c.c. per twenty-four hours.
   (c) Prevent the onset of or increase in degree of coma.
   (d) Produce a dilution of the blood as indicated by a decrease of at least 10 per cent in hemoglobin, cell volume, or serum protein concentration.

Eleven of the 12 maternal deaths were in these 13 patients as were 9 of the 18 infant deaths. Only 2 of the pregnancies in this severe group were less than 36 weeks in duration. In all but one instance, the fetal heart was present for some hours after admission. Prematurity was not an important factor in this group of infant deaths and they can be looked upon without additional exception, as due to the toxemia. There were no maternal deaths in the remaining milder 24 eclamptic patients, and of the 8 infant deaths, 6 were delivered before the thirty-sixth week of pregnancy.

The general plan of therapy in this series has been one of conservative medical management in an attempt to control the convulsions and establish an increasing urinary output. For this purpose sodium amytal in dosages from 3¾ to 7½ grains has been given intramuscularly at intervals of 3 to 6 hours dependent upon the response. This has been supplemented by the administration of magnesium sulfate in 100 c.c. of a 25 per cent solution intramuscularly repeated as necessary following convulsions. Rarely morphine sulfate gr. ⅙ to ¼ has been given although most of the patients have received morphine before admission to the hospital, and some have received either chloroform or ether inhalations during transportation to the hospital. Intravenous 20 per cent glucose in distilled water has been given in amounts of 1,000 to 1,500

c.c. repeated 2 to 3 times each 24 hours. Where this concentration failed to increase the urinary output, or where there was cardiac embarrassment or evidence of pulmonary edema, 30 per cent or 50 per cent glucose solutions in smaller amount has been used. Continuous oxygen by nasal catheter[2] has been given to most patients. Veratrum veride[3] has not been used. Following these procedures labor has been induced by rupture of the membranes alone or combined with the insertion of a bag, dependent upon the condition of the cervix or with the spontaneous onset of labor, it has been hastened by these procedures. Delivery has usually been performed under local infiltration or without anesthesia.

In all but the group of severe eclamptics, this general plan of management has proved effective. In the 13 patients with severe eclampsia, it has failed. Four patients died undelivered, 4 died following the delivery of stillborn infants. One patient survived following the delivery of a premature infant that died 18 hours after delivery. One mother and her infant survived. The remaining 3 infants survived following their delivery accomplished by cesarean section, which was in each instance performed upon a moribund patient. Six of the 12 maternal deaths were believed to be due to cerebral hemorrhage. This diagnosis was based upon the development of varying degrees of hemiplegia, but was proved by necropsy in only one instance. The remaining maternal deaths were associated with respiratory or cardiac failure superimposed on what are presumably irreversible metabolic changes of severe eclampsia.

It is my conviction that modification of our general plan of therapy would not have resulted in additional maternal or infant salvage. This group of severe eclamptic patients represents a failure of conservative treatment to produce any sort of satisfactory result. It is possible that any other plan of management would have been equally unsatisfactory. If we are to accept no other alternative as far as maternal salvage is concerned, there is certainly a possibility that a lessened infant mortality would result if more rapid delivery were accomplished. It seems justifiable with this in mind to undertake delivery by section in patients of this severe group. It is suggested that this be done as soon as possible following the initial establishment of conservative therapy. It is possible that termination may also result in the survival of some patients who might otherwise have been lost.

Various studies are recorded in the literature which indicate that the maternal survival is greater where operative interference is not undertaken. This is unquestionably true as regards any type of accouchement forcé. It is less definitely demonstrated in relation to cesarean section. Most reports of the use of cesarean section in the treatment of eclampsia are based on data collected more than fifteen years ago, and therefore, eliminate any improvement in technique that has occurred during that time. Most of them were sections done under general anesthesia.

Dieckmann quotes data from 3 large obstetric clinics showing that the maternal mortality increases from 7 per cent if delivery occurs within two hours of the first convulsion to 28 per cent if more than 21 hours elapse. He also states that, as a rule, where labor is slow, the eclampsia is likely to become more severe resulting in a higher maternal mortality. There seems no justification for the consideration of cesarean section in those patients with eclampsia who respond well to medical management and in whom labor progresses rapidly. There does seem to be justification for the consideration of it in those patients who fail to respond to conservative management and in whom the eclampsia had progressed to the severe stage.

The most satisfactory approach to the problem presented by this group of patients is the earlier recognition of the developing toxemia and the institution of adequate treatment before convulsions develop. It is significant in this connection, that in this series of patients with severe eclampsia, there had been little or no prenatal management. Many of them were seen by their local physician for the first time after convulsions had occurred. In all of the remainder the prenatal care had been inadequate. The majority of these patients came from an area essentially rural, and were of a relatively low economic level. They demonstrate the continuing need for additional public health and postgraduate medical education.

It seems logical to make the following conclusions from a study of this series of patients.

1. Conservative medical management followed by vaginal delivery is recommended for the treatment of mild eclampsia.

2. Adequate prenatal care, if it does not prevent the development of eclampsia, decreases the severity of the process and greatly improves the chance of survival of mother and infant.

3. Conservative treatment of severe eclampsia gives unsatisfactory results.

4. In severe eclampsia, the infant survival rate would be materially increased by the performance of cesarean section within a few hours following the institution of conservative medical management.

5. In severe eclampsia, the maternal survival rate is so negligible that the performance of cesarean section is justified in the interests of the infant and might be favorably influenced by the more rapid completion of the delivery.

6. Additional public health and postgraduate medical education is essential for the adequate prevention and control of eclampsia.

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A STUDY OF 250 CASES OF PLACENTA PREVIA*

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ALTHOUGH significant improvement in its treatment has been made in the past twenty-five years, placenta previa still remains one of the major obstetric problems, as little or no light has been shed upon its preventability, or etiology. That obstetrics is not an exact science, and cannot be practiced by formulas, can be no better illustrated than in the treatment of cases of implantation of the placenta in the lower uterine segment. In cases apparently identical in their inception, the end results with like treatment may be far apart. It is by interchange of experience among us that improvement is made, and even then what is one man's meat may be another man's poison, in so far as the application by the individual obstetrician of various procedures in treatment is concerned. It is with this in mind that I am presenting for your consideration and criticism, our experience for a period of ten years in the management of placenta previa.

Material

The material for this review is composed only of proved cases of placenta previa, and consists of patients encountered with this complication in a period of ten years, 1933 to 1942. In order that an adequate cross section of patients of widely varying economic and social status may be obtained, it is taken from the obstetric divisions of two hospitals, with different types of clientele. Harper Hospital is a private hospital with a small percentage of nonpay patients, while at Herman Kiefer Hospital, all cases are of the kind that require public assistance and are used for teaching purposes.

Incidence

A total of 31,996 deliveries occurred during the ten-year period, and among these placenta previa was encountered in 250, an incidence of 1 in 128. A high incidence is to be expected in hospital practice according to the reports of all observers.

TABLE I. AGE GROUPS

15 to 19	20 to 24	25 to 29	30 to 34	35 to 39	40 to
16	44	78	59	42	11

PARITY

I	*II*	*III*	*IV*	*V*	*VI*	*VII*	*VIII*	*IX*	*X*	*XI*	*XII*	*XIII*	*XIV*
49	59	41	22	32	13	6	11	7	3	0	4	2	1

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

The high percentage of cases (54 per cent) occurring in the age group 25 to 34 bears out the commonly made observation, that placenta previa occurs most in the middle childbearing period.

Our material shows that placenta previa occurs about five times as often in multiparas as in primiparas. In private hospital practice, the condition is more common in primiparas than in clinic practice. Thirty-nine cases occurred in primiparas in the former group of 101, while only 10 of 149 cases were primiparas in the clinic group.

Placenta previa seems to be more prevalent among whites. Of 250 cases only 51 occurred in colored women, in spite of the fact that our nonpay patients are comprised of a high percentage of colored.

TABLE II. LOCATION OF PLACENTA

Marginal	133
Lateral	67
Central	50
Total	250

The difficulties associated with making an accurate classification of placenta previa, according to location, need no elaboration to a group of experienced obstetricians. Every effort has been exerted in the attempt to have our grouping as nearly correct as possible. We find that 53.2 per cent were marginal, 26.8 per cent were lateral, and 20 per cent were central.

While every means advisable is used to make a correct diagnosis of the location of the placenta, we believe that the amount of blood lost, or being lost when the patient is first seen, should be a better guide to treatment than the amount of os covered by the placenta. In our experience, more blood is lost, at times, with the marginal than with the central type.

TABLE III. CONDITION OF PATIENT

	GOOD	FAIR TO POOR	VERY POOR
Vaginal delivery	90	78	23
Cesarean section	42	16	1
Total	132	94	24

Of paramount importance in treatment and prognosis, is the condition of the patient when first seen. Table III gives our estimate in the 250 cases studied. Those classified as "Good" had no serious blood loss, as shown by clinical observation, pulse rate, blood pressure, blood count, hemoglobin readings, etc. Those called "Fair to Poor" have had sufficient loss of blood so that their condition can readily be discovered clinically, and confirmed by laboratory findings. We have classified as "Very Poor" those patients entering in really serious condition with massive blood loss, marked pallor, rapid thready pulse, frequently with air hunger, with hemoglobin readings below 50 per cent,

and with marked drops in blood pressure. I believe it is significant that of the women treated by cesarean section, only one case was in this "Very Poor" group.

Symptoms and Diagnosis

Painless, causeless bleeding, particularly if occurring in the last trimester of pregnancy, is the classical symptom, and has been invariably present.

I do not believe it necessary or advisable to confirm a diagnosis of placenta previa in all cases by vaginal examination; and particularly in those in which delivery by cesarean section is contemplated. A sufficiently accurate working diagnosis can be made in many instances by other means.

Two aids to diagnosis I have found to be of considerable help; viz., the location of the placental souffle, and the use of the x-ray.

If heard best low in the abdomen above the symphysis, in cases with suspected placenta previa, I think the location of the placental souffle to be of considerable significance. While attempts are always made to locate it, these are easily omitted from the written record which accounts for the fact that I have record of them in only 71 cases. Of these, it was heard low above the symphysis in 59, and not heard in 12.

X-ray diagnosis was attempted in 32 cases, proved to be placenta previa, by the use of an opaque medium in the bladder, or by the soft tissue technique. In 24, a positive confirmatory diagnosis of placenta previa was made, in 3 the diagnosis was questionable, and in 5 negative. A correct diagnosis was made in 75 per cent of patients.

TABLE IV. METHOD OF DELIVERY

Vaginal 191	
(A) Expectancy	58
(B) Rupture of membranes	26
(C) Bag insertion	105
(D) Braxton Hicks' version	2
Cesarean Section 59	
(A) Classical	10
(B) Low cervical	44
(C) With supravaginal hysterectomy (Porro)	5

It is evident from Table IV, that widely varying methods of delivery have been used. This I think is to be expected in any series of cases that represents a true sampling of a large metropolitan population. Our patients come from all social and economic levels, and their condition when first seen precludes treatment of a single type. In this connection it is interesting to note that in 101 placenta previa cases from Harper Hospital, cesarean section was the treatment of choice in 41, while in 149 cases from the Herman Kiefer service, only 18 cases of section occurred.

Patients of private physicians, who have had adequate prenatal care, and who are seen with the first bleeding are much more likely to be

candidates for section, than nonpay patients who frequently enter in serious condition. All the more is this likely to be true if the patients are paras i or ii, at or near term, with both mothers and babies in good condition.

Four of six attending obstetricians at Herman Kiefer Hospital also do their private obstetrics at Harper Hospital, enough I think to appreciably influence the trend of treatment over a period of ten years. And yet, these men, who have a comparatively high cesarean rate in private practice, do not throw their influence toward a higher rate at Herman Kiefer Hospital. Again the answer is found in the types of material encountered, regardless of the comparative simplicity of treatment by the abdominal route. That good results for both mother and child with cesarean section are obtained, will be shown in our mortality tables, but only, I believe, when we do not overstep the bounds of sound surgical judgment.

Preference for the low cervical operation is marked, 44 of 59 cesarean sections being of this type. There have been no serious technical difficulties and we agree with Greenhill and others, that at times, the low incision is of distinct advantage in the control of bleeding from the placental site.

In delivery by the vaginal route, "expectancy" was chosen as most appropriate for 58 mothers and 59 babies. By expectancy we mean that no active treatment, aimed at delivery, was instituted, and labor was allowed to continue, under close observation, until complete dilatation of the cervix. From then on, labor was terminated according to indication. Thus, spontaneous delivery occurred in 40, forceps in 10, version and extraction in 5, and breech extraction in 4. Of 26 patients in whom rupture of the membranes was the only active treatment in the stage of dilatation, labor terminated spontaneously in 11, forceps were used in 2, version and extraction in 8, and breech extraction in 5.

The insertion of the dilatable bag for control of hemorrhage, and to aid in dilatation was thought to be the best treatment for 105 women, and 110 babies. After which delivery was spontaneous in 64, forceps delivery was done in 9, version and extraction in 14, and breech extraction in 18.

I am fully aware of the criticisms that have been aimed at the use of the bag and its many supposed disadvantages, such as predisposition to malpositions, inefficiency in control of hemorrhage, infection, etc., and can only say that these have not occurred to an extent to discourage us in its continued use. Malpositions after the use of the bag have occurred so infrequently, as to be statistically unimportant. Control of hemorrhage has been excellent, and I have found no case of failure while the bag was in situ. While infection is a well-known complication of placenta previa, in general, I have found no increase in morbidity after the

use of the bag as compared with other methods of treatment with delivery from below.

On the other hand, I am confident that in many cases entering as emergencies, with massive blood loss and profuse bleeding, the insertion of the bag has controlled hemorrhage to permit of blood transfusion and other supportive measures which have been lifesaving. It is of little use in these cases to allow the patient to lose blood faster than it can be replaced. The use of the bag is a more exacting form of treatment from the viewpoint of the obstetrician than is cesarean section, as it requires constant attention to detail and indefinite periods of waiting for its expulsion. Serious bleeding can occur above it, unobserved externally, if it is not promptly removed once its purpose is served. Of value in vertex positions, particularly, is the use of small doses of pituitrin, once the bag is removed, to help wedge the head firmly against the placenta, or careful version and slow extraction can be done to advantage in many cases. If the placenta does not separate immediately it is removed manually, followed frequently with the insertion of a gauze pack.

I have no fault to find with the obstetrician who can limit his treatment of placenta previa to simple rupture of the membranes and cesarean section. As has been seen, we use both these methods. However, in our material, there is a group of cases which is not suitable for either of these; for them we use the dilatable bag.

TABLE V. MORBIDITY AND MORTALITY

By the commonly used criteria 78 cases were morbid post partum, 31.2%; maternal mortality, 7—2.8%; vaginal delivery, 6—3.1%; cesarean section, 1—1.7%.

PARA	DURATION	CONDITION	DILATATION	PLACENTA	TREATMENT	CAUSE OF DEATH
(1) iv	6½ mos.	Very poor	Complete	Centralis	Rupt. Memb. V & E	Transfusion reaction
(2) iv	7 mos.	Very poor	Complete	Centralis	Rupt. Memb. Spont.	Hemorrhage
(3) iv	9 mos.	Fair	4 cm.	Lateralis	Bag, V & E	Not known, autopsy, Anesthetic (?)
(4) iii	9 mos.	Poor	2 cm.	Centralis	Low cervical section	Acute dilatation of heart, circulatory collapse
(5) vi	9 mos.	Poor	5 cm.	Lateralis	Bag, Breech ext.	Hemorrhage
(6) ii	6½ mos.	Fair	4 cm.	Lateralis	Bag, V & E	Hemorrhage
(7) iii	8 mos.	Very poor	6 cm.	Centralis	Bag, Breech ext.	Septic pneumonia 12th day

A total of 7 cases died, 6 after vaginal delivery, and 1 after low cervical cesarean. Reference to Table V will show, in more detail, the facts pertinent to these cases. One case dying after transfusion, and one probable anesthetic death possibly could have been avoided. In the case of the posttransfusion death, the Rh factor was not determined which, in the light of later knowledge, might have accounted for it.

Of the total of 250 cases delivered, 263 babies were born. There were 13 twin pregnancies, and 4 malformations incompatible with life, a high incidence, confirming the experience of most writers—91 babies did not survive, a gross mortality rate of 34.6 per cent.

There were 56 neonatal deaths, of which 31 were nonviable prematures, and 3 had malformations incompatible with life.

Thirty-five babies were stillborn, of which 18 were nonviable prematures, and 1 had malformation incompatible with life.

TABLE VI. FETAL MORTALITY

Total deliveries:	263
Total deaths:	91
Gross rate:	34.6%
Neonatal deaths:	56
Nonviable prematures	31
Malformations	3
Total nonviable	34
Stillborn:	35
Nonviable prematures	18
Malformations	1
Total nonviable	19
Net fetal death rate	14.4%

It is a questionable procedure to arrive at a net fetal mortality rate for placenta previa, because prematurity and fetal malformations are an inherent part of the risk in this complication of pregnancy. However, if the usual practice is followed and the above deductions are made from the gross death rate, it is found that 34 babies born alive and 19 stillborn were nonviable, a total of 53. Thus, the net fetal death rate is 38 or 14.4 per cent.

Discussion

No discussion of placenta previa in modern times is complete without reference to blood transfusion, and the use of blood plasma. Their use with us is so common as to be routine in all but the mildest cases of bleeding. Patients have received at times, before, during, and after delivery, as much as 3,000 to 3,500 c.c. of blood. While plasma is very valuable, it does not fill the place of whole blood in cases with massive hemorrhage. There is considerable time consumed in typing, cross-matching and Rh factor determination while the patient continues to bleed. The use of plasma during this period is a valuable adjunct. At times, washed red cells have been used. All cases of suspected placenta previa should have the benefit of hospitalization, and blood for transfusion should be available for them. Bill of Cleveland was among the first to call our attention to the reduction in mortality possible when these conditions are fulfilled.

Apparently, the best results in the treatment of placenta previa are obtained by the obstetrician in the care of his private patients (mor-

tality 1.9 per cent). The intelligence of the individual patient is an important factor. Many tragic cases are the result of failure of the woman to report mild bleeding in the last trimester to her clinic or to her physician.

We have had no experience with Willetts' scalp traction but from the reports of experienced observers, believe that it has merit in properly selected cases, and intend to try it when the opportunity presents itself. One academic objection to its use in the case of prematurity might be the difficulty of application of the forceps to the snugly fitting scalp of a premature infant.

In studying placenta previa in a metropolitan area, I believe it important that sampling, as widely as possible, in all social and economic strata, be done. For this reason, material from two hospitals with widely varying types of clientele has been studied. This analysis shows marked difference in treatment, especially in the use of cesarean section. That this occurs with staffs that, to a large extent, are interlocking, and where the attending obstetrician is free to exercise his own best judgment, leads to the conclusion that treatment must vary greatly with the conditions encountered, considered in the broadest sense. I believe that each case should be individualized. The obstetrician should have an open mind, free from prejudice in favor of one or another form of treatment. Treatment should conform to the immediate need of the patient, and should not be based on preconceived ideas of the operator.

Summary

For a ten-year period, 1933 to 1942, there were 31,996 deliveries at Harper and Herman Kiefer Hospitals, among which there occurred 250 cases of placenta previa, 1 in 128.

Placenta previa is found in primiparas and multiparas in the ratio of 1 to 5.

It is more common in whites than colored.

It occurs most commonly in the middle childbearing age.

A high percentage of twin pregnancies and fetal malformations is to be expected.

A large group was satisfactorily managed by expectant treatment during the stage of dilatation, or by simple rupture of the membranes.

The insertion of the dilatable bag gives good results in cases adapted to its use.

In properly selected cases cesarean section can be used to the advantage of both mother and child.

Seventy-five per cent of cases were correctly diagnosed by x-ray in the group in which it was used.

Blood transfusion should be available to all patients with placenta previa. An acceptable mortality rate cannot be expected without it.

Maternal mortality in 250 cases of placenta previa taken from a large metropolitan area was 2.8 per cent.

Gross fetal mortality was 34.6 per cent, net 14.4 per cent.

1551 WOODWARD AVENUE

Discussion

DR. T. K. BROWN, St. Louis, Mo.—Cases of pregnancy with painless, causeless uterine hemorrhage in the last trimester should be hospitalized as soon as possible with the tentative diagnosis of "Placenta Previa." The diagnosis should be confirmed promptly by history, physical findings and perhaps roentgenological methods. Treatment should be instituted at once with the following purposes: (1) arresting hemorrhage; (2) emptying the uterus as promptly as is safe; (3) insuring control of hemorrhage after delivery; (4) counteracting anemia; (5) preventing infection.

Hemorrhage may be arrested by the administration of vitamin K, rupture of the membranes, insertion of a bag or cesarean section. The uterus may be emptied as promptly as is safe by rupture of the membranes, insertion of a bag or cesarean section. Hemorrhage after delivery may be controlled by drugs, packing, and perhaps suture of the placental site. Anemia should be counteracted by the transfusion of Rh negative blood before, during, and following delivery. Plasma transfusions may be used to combat "shock" but do not supply the necessary cellular elements to correct the anemia. Infection may be prevented by the use of proper technique, administration of vaginal antiseptic instillation, limitation of interference to a minimum, and removal of any pack in eight to ten hours.

Watson and Gusberg have recently reported definite improvement in maternal and fetal mortality and maternal morbidity by the use of cesarean section in the treatment of placenta previa in comparison with their results following use of the bag.

In the analysis of Dr. Seeley's cases, central placenta previa was encountered in 1 out of every 5 cases. In such cases, delivery by cesarean section is the method of choice.

As to the condition of the patients when first seen, 20 per cent were classified as "very poor" but only one case in the group was delivered by section. Would it not have been possible to have improved the condition of these patients by proper treatment and then to have delivered some of them by cesarean section?

Over 50 per cent of this series of cases was treated by the insertion of a bag. I still fear the danger of infection associated with the use of a bag. The fetal morbidity for the 250 cases reported was 31.2 per cent. Was there any difference in morbidity in the group that was "bagged" as compared with the remainder of this series?

Marginal placenta previa was reported in 133 patients. Nevertheless, only 26 cases were treated by rupture of the membranes. It would seem that this method of treatment could have been employed frequently.

Among 101 private patients, of whom 39 were primigravida, 41 cesarean sections were performed. These patients were in good condition and the results could be expected to be satisfactory. In contrast, among the 149 clinic patients, of whom 10 were primigravida, only 18 cesarean sections were performed. Perhaps in this latter group the indication for cesarean section could be broadened and used as the method of delivery after proper prophylactic treatment.

Low cervical section was performed in 44 instances among the 59 cases delivered by section. One must consider the increased hazard of encountering the placental site at operation in this particular group of cases. The loss of blood may be

increased definitely and perhaps to a dangerous degree. By the use of classical section this difficulty may be obviated. However, the placental site might be sutured, if necessary, more readily after low cervical section. Postpartum bleeding can usually be controlled by the use of a pack.

Dr. Seeley and his co-workers are to be complimented on their satisfactory maternal mortality rate of 2.8 per cent and should continue to individualize the treatment of their cases of placenta previa in the future.

DR. EDWARD A. SCHUMANN, Philadelphia, Pa.—The whole subject of placenta previa continues, even after the hearing of this excellent paper, in my mind as the most confused chapter in obstetrics. Neither the cystogram with an opaque medium nor the soft tissue x-ray has proved satisfactory as a diagnostic method in our hands except as corroborative evidence in well-established cases. The diagnosis by vaginal examination has even offered difficulties to me. If one passes a finger through the cervical canal one can tell, but who dares? As to the difference between a lateral and marginal position, this is often merely an academic decision.

When we come to the subject of treatment the chapter becomes still more confused. I would be very happy to have outlined to me the treatment of placenta previa in a woman six and a half months pregnant who desires a child. I know of no satisfactory treatment except expectancy, which sometimes is feasible and sometimes not. Given the case of a primipara shortly before the viability of a child, when the child is desired by both parents, I think it is the duty and necessity of the obstetrician to lay the dangers of expectant treatment clearly before the parents and have them make the decision as to whether the woman should be permitted to go on with her pregnancy facing the danger of a severe hemorrhage. The full responsibility should be placed on the parents.

As to the treatment of placenta previa after the viability of the child, I would accept the form of treatment that best suits the capability of the obstetrician. In my own cases, I am more influenced by the condition of the cervix than any other factor. Given a soft or partially dilated cervix I believe any of the methods of treatment will be successful and will give the excellent results produced by Dr. Seeley. Where the cervix is dense and does not render itself easily dilatable, I think cesarean section is the only method. In a member of my own family, cesarean section would be practiced almost invariably with a viable child and a placenta previa.

DR. JOSEPH L. BAER, Chicago, Ill.—I have been waiting for some one to emphasize the fact that obstetric hemorrhage has displaced puerperal infection as the number one cause of maternal deaths in the United States. Not having heard it, I again bring it to attention. For many years all of the specialty societies, including this one, have been emphasizing the educational needs for the prevention and treatment of puerperal infection, which now has taken second place. It now behooves us to embark on a more vigorous program of education for the men in general practice who are the ones to see the patients with premature separation of the placenta and placenta previa. We must emphasize first the extreme importance of bleeding in the third trimester of pregnancy so that those patients will be immediately hospitalized and be given the benefit of early expert consultation. If that can be accomplished, we will definitely lower our maternal mortality from obstetric hemorrhage.

Vaginal examination is not merely permissible but highly desirable. Of course, in the delivery room precautions must be taken against the possibility that the examination will precipitate further bleeding. The sensation given by a thickened area in the lower uterine segment between the finger and the presenting part, which in these patients can usually be impressed into the pelvis, since the infants are so frequently premature, is definite evidence of the low implantation. Subse-

quent treatment then is a matter of individual choice. In many instances simple rupture of the membranes with adequate drainage of the liquor amnii should take precedence over the abdominal approach.

DR. F. H. FALLS, Chicago, Ill.—I should like to ask how one would differentiate between placenta previa and carcinoma of the cervix without a vaginal examination? X-ray in placenta previa in our hands has been very unsatisfactory.

Inserting a bag to facilitate the delivery in placenta previa increases the danger to the fetus from compression of the placenta by the bag. This is particularly so if the cord happens to be inserted at the lower side of the placenta, for in that event when the bag is blown up, you stop the circulation of the cord.

When doing a low cervical cesarean section for placenta previa, you may cut through the placenta and thus divide the large vessels of the fetal surface. This is analogous to cutting the baby's throat, and from under such circumstances you have to hurry to get the baby out and the cord clamped in order to prevent bleeding. This is an important cause of fetal death. In a good many of these cases there may be justification for doing a classical operation thus avoiding injury to the placenta by the knife.

My last point concerns the cause of the bleeding in placenta previa. We think it is associated with the contraction of the uterus and the formation of the lower uterine segment. We believe that if there were a way of stopping the contractions, we might reduce the chances of full separation of the placenta. In the last five or six years, therefore, we have been giving progestin until viability of the baby was attained and then doing a cesarean section.

DR. FRED L. ADAIR, Chesterton, Ind.—The advocacy of expectancy or delay in treating placenta previa is extremely hazardous, and if generally adopted would lead to an increased mortality. It should not be carried out under any circumstances except in a special hospital and with expert care.

We have felt at the Chicago Lying-in Hospital that rectal examinations are never justified in placenta previa and that when a vaginal examination is made, it should be done as promptly as possible with everything in readiness to take care of the case by the most expert treatment. In many cases, however, the very simple procedure of rupture of the membranes is of great value in the management of these cases.

DR. GEORGE W. KOSMAK, New York, N. Y.—In closing I would like Dr. Seeley to state whether the insertion of the bag was extra- or intraovular.

DR. SEELEY (closing).—In advocating the use of the dilatable bag, I might remind you that the majority of our cases in which it was used were brought to us by ambulance and showed more than 4 cm. of cervical dilatation. A large proportion of them are multiparas and I do not know any way of controlling the hemorrhage except by the use of the bag. If you could see our material I think you would doubt that they were cases for cesarean section.

Replying to the question as to infection after the use of the bag, I would say that we have not been able to show any more morbidity with the use of the bag as compared with other methods for delivery from below. All of our men except one have favored the use of the intraovular bag. The extraovular bag has been used in a certain percentage of these cases, the argument being, of course, that the extraovular bag would be likely to give a lower percentage of fetal deaths.

AN ANALYSIS OF STERILITY STUDIES IN THE FEMALE*

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THE problem of sterility is an age old one, as is evidenced by the frequent references to barrenness in the biblical literature and there are probably few afflictions that cause as much anxiety and unhappiness as does this condition. It has been estimated by Reynolds, Macomber, and Lotka that 13 to 17 per cent of the marriages in this country are barren. This seems like a high incidence in these days of scientific achievement and in this world of plenty. Nevertheless, it is true and should serve as a real incentive to the medical profession to put forth every effort to correct and overcome, in so far as is humanly possible, the varied causes of sterility.

Prior to 1920, sterility studies in the female were often cursory and not too scientific. The usual procedure then, was a pelvic examination to determine and correct, if present, any uterine displacement. Often a dilatation and curettage was carried out, but not for any sound scientific reason. Little emphasis was placed on the male as a possible causative factor. But all these things have changed and in the last quarter of a century, more has been accomplished to overcome sterility than in all the centuries preceding it.

The world of today is especially in need of an increased number of births, to replace those that have and will be called upon to make the supreme sacrifice to bring us total victory. So we feel that every one of these discouraged couples, that come to us with their problem of infertility, should be given the greatest consideration and the benefit of our best and most complete scientific investigation.

The purpose of this presentation is to analyze a group of seventy-six women, who were admitted to our clinic at the Geisinger Memorial Hospital in the two-year period ending July 1, 1943, with the chief complaint of inability to conceive.

All but five of the husbands of these women, were examined by our urologist or by a competent physician elsewhere prior to the admission of their wives for studies. Of the remaining seventy-one husbands, sixty-eight, or all but three, were reported as having an ample number of motile spermatozoa with good morphologic characteristics, which according to Rubin and others, pretty nearly exonerates the male from being responsible for the infertility. The probable causes for the sterility in the three husbands pronounced infertile were reported as chronic prostatitis, absence of spermatozoa, and diminished motility of spermatozoa with a high incidence of abnormal forms, respectively.

Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

These findings do not seem to bear out the works of Mazer, Israel, and Charny who found in their series that 40.6 per cent of the male partners had various types of semen abnormalities and, therefore, were potentially a factor in their barren marriages.

Suffice it to say that the sixty-eight husbands who were reported to have normal semen received no therapy. The three husbands, who were found infertile received active treatment for a long period of time on the urological service and it is interesting to note, that to date, no pregnancies have resulted in these three couples.

From this point on, our chief concern on the gynecological service was the study, evaluation of our tests, and the treatment of these seventy-six women admitted to our hospital complaining of infertility. Their ages varied from 21 to 38 years, the average age being 28.3 years. The period of marriage varied from 1 to 19 years, or an average of 5.8 years. The period of infertility varied from 1 to 19 years and the average for the group was 4.9 years. Two patients showed evidence of anemia and only one had a positive serologic test. Of the entire group, only 21 patients gave a history of irregular menses or menstrual disturbance. Twenty-one patients had one previous pregnancy which resulted either in a full-term baby or abortion followed by at least two years of sterility.

A careful pelvic examination by palpation and inspection was carried out in each instance and the following conditions were revealed.

TABLE I. PELVIC FINDINGS

1. Normal pelvis	45
2. Genital hypoplasia	8
3. Retroversion	4
4. Uterine fibromyomata	3
5. Adnexal pathology	13
6. Cervical stenosis	3
Total	76

Three of the patients had previous pelvic surgery which may or may not have played some part in their sterility. From these examinations, it would seem that 45 patients or nearly two-thirds of the series had normal pelvic organs, as far as could be determined, by manual palpation and inspection. Those patients with genital hypoplasia were treated with estrogenic substance and thyroid extract. The four patients with retroversion had manual correction and pessaries were inserted. The three patients with a diagnosis of fibromyomata were advised at least for a time against surgery because of the small size of the tumors.

The diagnosis of adnexal pathology occurred thirteen times and included cystic ovaries, thickened and fluctuant Fallopian tubes, but no evidence of any acute pelvic inflammatory disease. None of these existing adnexal conditions had caused the patient enough pain or distress to have suggested their presence, nor were they of such a

nature that surgical measures would likely have lessened their sterility. Cervical stenosis occurred in three patients and all were dilated with graduated dilators.

An attempt was also made to classify the entire group according to endocrine status and the following table represents this correlation.

TABLE II. ENDOCRINE STATUS

1. Normal	24	31.5%
2. Hypothyroidism	36	47.4%
3. Pituitary dysfunction	5	6.6%
4. Ovarian dysfunction	11	14.5%
Total	76	100.0%

Of the group, 24 had no symptoms nor physical evidence of any endocrinopathy.

Hypothyroidism comprised the largest single group, in fact almost half of the entire series. It is interesting to note, that in most instances, we were able to pick out the hypothyroid cases simply by careful interrogation before the basal metabolic determinations were computed. These patients have a definite syndrome and practically all of them had the characteristic signs and symptoms of fatigue, lack of energy, sensitivity to cold, inability to get up in the morning feeling rested, dry, lusterless, and straw-like hair, deficient vaginal secretions, and absent or diminished libido. The basal metabolic determinations for these patients were characteristically low, varying from –7 per cent to –33 per cent, the greater number varying between –15 per cent and –20 per cent. Twenty-nine of the 36 hypothyroid patients had basal metabolic rates below –10 per cent and the other 7 patients had rates varying between –10 per cent and 0. It may be said here, that in our opinion, a –10 per cent basal metabolic rate, which is considered a low normal by most schools, is in reality quite subnormal and clinically capable of producing the characteristic hypothyroid syndrome, with the resultant sterility. Therefore, for all practical purposes, the minimum normal basal metabolic rate should more nearly approach zero. The treatment prescribed for the hypothyroid group was desiccated thyroid extract grs. ss b.i.d. to grs. I t.i.d. varying with the size of the patient, severity of symptoms, and the degree of subnormal basal metabolism.

The five cases diagnosed pituitary dysfunction, presented the typical pelvic and shoulder girdle adiposity and in each instance their weight considerably exceeded that of all others in the series. One patient received x-ray radiation of the pituitary at another hospital. Two patients received a series of gonadogen injections, and one patient refused treatment while the fifth one had regular menses and no hormone therapy seemed indicated.

The ovarian dysfunction group totaled eleven patients, eight of whom had definite hypoplastic genitalia and, in most instances, had

menstrual irregularities. These patients received estrogenic therapy in the form of stilbestrol 2.0 mg. three times a week and small doses of thyroid extract in the amount of grs. ss t.i.d.

The hysterosalpingogram was done on twenty-one patients to determine patency of the Fallopian tubes with the following results.

TABLE III. HYSTEROSALPINGOGRAMS

DIAGNOSIS	NUMBER	SUBSEQUENT PREGNANCIES
1. Patent tubes	10	6
2. Occlusion of one tube	3	2
3. Occlusion of both tubes	7	1
4. Partial stenosis	1	1

The incidence of pregnancy which ensued in this group, when the uterosalpingogram was done, seemed quite high and possibly cannot have too much importance attached to it because of the small number in the series.

Tubal insufflation, or the so-called Rubin test, was performed on forty-five patients and the following kymographic interpretations were recorded.

TABLE IV. TUBAL INSUFFLATIONS

DIAGNOSIS	NUMBER	SUBSEQUENT PREGNANCIES
1. Patent tubes	19	7
2. Partial stenosis	8	1
3. Bilateral occlusion	17	1

Many of these patients had repeat tubal insufflations but these are not recorded, since for practical purposes, the management of each case was carried out with respect to the initial findings. However, from the comparison of the uterosalpingograms and the tubal insufflations, disregarding the relatively small series, the former was followed by a much higher incidence of pregnancy which was not at all evident to us until this analysis was carried out.

Endometrial Biopsy

In recent years, we have learned that endometrial biopsies can be most helpful, and thus, should be an integral part of every investigation for sterility in the female. It is our practice to arrange admission of the patient for her sterility studies two or three days before the expected menstrual flow, in so far as is possible. In this way we feel, that if the patients have ovulated, it can be verified by the microscopic picture of the luteal phase in the biopsies, and thus rule out anovulatory menstruation as a possible cause of the sterility. It must be remembered, however, that many of the patients who present themselves for study have very irregular menses or possibly amenorrhea, for a long period of time. It is, with this type of case, that the endo-

metrial biopsy is of doubtful value since it permits no correlation of the menstrual cycle, and, therefore, our efforts must first be directed toward the establishment of a regular cycle with rythmic bleeding. This we have accomplished in a few instances by the administration of gonadogen, synopodin, and prostigmin sulfate but not with sufficient success to herald it widely.

In concluding our studies and arriving at the final analysis, it was necessary to contact 27 of the 76 patients by letter and a questionnaire to determine our results, because of their failure to return for their follow-up examination. A few of these had become discouraged and consequently had discontinued their medication, but for the most part the reports were encouraging. The other 49 patients were most cooperative in aiding us in this study, even though it required traveling rather long distances every two or three months for follow-up examinations.

Table V, with the cases arranged according to endocrine status, shows our end results in the number of pregnancies obtained, including both full-term babies and spontaneous abortions.

TABLE V. INCIDENCE OF PREGNANCIES

ENDOCRINE STATUS	NUMBER	TOTAL NO. OF PREGNANCIES	FULL-TERM PREGNANCIES	SPONTANEOUS ABORTIONS
Normal	24	4	4	0
Hypothyroid	36	19	17	2
Pituitary dysfunction	5	0	0	0
Ovarian dysfunction	11	6	5	1
Totals	76	29	26	3

From these findings it is quite clear that the hypothyroid and ovarian dysfunction groups, which together total 47 patients, lend themselves well to simple therapy, as is shown by the total of 25 pregnancies that resulted, an incidence of slightly better than 50 per cent. In contrast, the pituitary dysfunction group, which was small, had no resulting pregnancies and the patients showed no benefit or improvement from our medication. In the normal group of 24 patients our results were a little better, but far from satisfactory. The women in this group probably cause us more concern than all the rest put together, for the reason that they appear perfectly normal and show none of the characteristic signs and symptoms so common in endocrinopathies and, if after eliminating such causative factors as occluded tubes, fibromyomata, etc., we have only to accept an inherent low fertility factor as the probable cause of their sterility.

We have been especially impressed with the treatment of our hypothyroid and hypoovarian groups with thyroid extract. While we know it is a form of therapy, that has been used for years and was stressed by Litzenberg in 1937, in carrying out studies on a similar series and with comparable results, yet we feel that there are many

more hypothyroid patients than most medical men are willing to admit and that the greatest number of patients to benefit and overcome their sterility is dependent upon the physician's looking more carefully into the patient's metabolic condition and resorting less often to the diagnosis of psychoneurosis. It has been our experience even though many of these hypometabolic patients may never conceive, they do improve both physically and psychically on thyroid therapy and, thereby, usually become better partners in marriage.

Summary

1. An analysis of seventy-six cases of sterility in the female.

2. The studies that afforded us the greatest information as to the cause of the sterility were basal metabolic determinations, hysterosalpingograms, and tubal insufflations.

3. The greatest number of pregnancies occurred in the hypothyroid and ovarian dysfunction groups that received thyroid extract, estrogenic therapy and/or follicle stimulating hormone.

4. Of seventy-six cases studied and treated, a total of twenty-nine pregnancies resulted, three of which terminated in spontaneous abortion, and the remaining 26 were delivered as normal healthy babies.

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Discussion

DR. I. C. RUBIN, New York, N. Y.—A number of interesting phases of sterility and infertility, which have become increasingly appreciated by gynecologists and the general profession in the past 25 years, have been presented in this paper. Some of the observations and conclusions, however, are at variance with the experience of other workers in this field and are therefore noteworthy. For example, a very small percentage of male infertility was encountered. Only 3 out of the 71 husbands were regarded as infertile according to the urologist's estimate of the seminal contents. The criteria of what constitutes normal semen vary considerably. Some are content to call many specimens normal, while others might regard the same specimens inadequate.

Despite Hühner's important contribution made over thirty years ago, and much work that has since been done by Moench and others on the morphological types of spermatozoa, there is as yet no unanimity of opinion as to the percentage of abnormal sperm compatible with fertility. The Hühner test has proved itself to

be a simple clinical method which enables us to ascertain the reaction between spermatozoa and the female genital secretions at their first encounter and incidentally determines the mechanical potency of the husband as well as his ability to produce spermatozoa.

The examination of the condom or unmixed specimen of semen is not entirely conclusive. It should be preceded or at least followed by the Hühner test which affords a truer estimate of the fitness of the spermatozoa. Their essential viability and virility are roughly estimated by their survival in the vaginal and cervical secretions, the only other natural environment they are destined to live in after being discharged from their source.

Even the finding of an adequate number of viable sperm in the vagina and cervix does not wholly exonerate the husband from the cause of the sterility, as Hühner and many of us at first believed. In the final analysis, the only real test of the fitness of the male gametes is their power to impregnate an ovum which eventually develops into a healthy living baby. Our results in combating childlessness may be expected to improve the more we are prepared to investigate the causes of the infertile mating rather than the infertile individual, devoting as much attention to the male as to the female partner.

It is only possible for me within the limited time allowed for discussion of this many faceted problem to take up one or two other essential points brought out in the paper. The endometrial biopsy gives information concerning a single menstrual cycle, but this does not necessarily hold for other cycles. I hesitate to take an endometrial specimen just before the onset of the menses for fear of interfering with a possible early pregnancy in a group of women to whom a single conception is precious.

The cases with hysterosalpingography and tubal insufflation in the series are, as Dr. Nicodemus has stated, too small in number to permit of broad deductions. It is quite possible that the percentage of pregnancies with respect to each method might be appreciably changed in a larger group. In my own series this has been found to be so.

The clinical diagnosis of hypothyroidism in connection with the basal metabolic rate has brought the most successful results in the series just reported. The rather large proportion of patients with hypothyroidism, as reported today, suggests differences in the subgroups met by others, which may account for the difference in therapeutic results. Chance and coincidence, even geographic location, play a not insignificant part in any analysis of therapeutic results, especially in sterility.

The fact that only 4 became pregnant of the 24 patients who were classified by the authors as normal from the endocrinologic point is difficult to explain, because 85 per cent of marriages in the general population prove fertile. Detailed analysis of all ascertainable factors might account for this fortuitous group. But it illustrates what a complex problem human sterility and infertility is despite the progress which has been made in our time. There still remains a relatively large group of sterile matings, with and without recognizable deficiencies, which defy all our efforts to relieve.

DR. KARL M. WILSON, Rochester, N. Y.—I would like to enlarge a little on the problem of determining the time of ovulation, particularly in those women who present a somewhat irregular cycle. In my clinic at the Strong Memorial, we have been devoting considerable attention to this angle of the problem in the last few years. When one has to deal with an irregular cycle, unless endometrial biopsy be taken at a particularly fortunate time, whether ovulation occurs, or when it occurs cannot be satisfactorily determined. There are a number of possible observations however, of which none is absolutely conclusive alone, but which taken together may prove of value in determining this point. These include the slight spotting which may occasionally be observed at the time of

ovulation if careful watch is kept; a rise in estrogenic hormone in the blood, which, of course, would require numerous and repeated observations; an increase in the pregnandiol excretion which may be taken as an indication of an active corpus luteum; also the vaginal smears, which, as emphasized by Traut, show an increase in leucocytes and cornified cells, less mucus and possibly erythrocytes at the approximate time of ovulation. Seguy and his collaborators have found an increase in the glairy cervical secretion in the midinterval of normal women followed by desquamation. Lamar has further shown that cervical mucus is under these conditions permeable to spermatozoa but not at other times. If temperature readings are carefully and accurately made throughout the cycle there is a sharp rise of about 0.3 of a degree F. just before or after ovulation. A rise of 0.3 in the pH of the vaginal secretion has also been noted at the approximate time of ovulation.

All these findings are of course only approximations but taken together they may be helpful in those who present irregular cycles and in whom it is therefore difficult to determine whether ovulation does occur at all, or if it does occur at just what time. Having obtained this information, an endometrial biopsy at the selected time will give us the final information.

DR. BENJAMIN P. WATSON, New York, N. Y.—Emphasis should be put upon the low basal metabolic rate in many of these sterility cases. We ought in particular to be careful about the dosage of thyroid. One so often finds a patient who comes in with a definite history of a low basal metabolic rate and discovers that she has been getting a half grain of thyroid a day. If there is a low basal metabolic rate, adequate doses of thyroid should be given and adjusted in accordance with further basal metabolic rate determinations. Most of these patients can take as much as three or four, or even five, grains of thyroid a day before any result is seen. Furthermore, we should pay as much attention to the basal rate of the husband as of the wife. It is my practice to give the husband the same therapy as the wife if his basal metabolic rate is low.

DR. J. C. LITZENBERG, Minneapolis, Minn.—I am certainly gratified to find that my results reported in 1937 still pertain, and that a low basal metabolic rate is an indication of hypothyroidism and also hypo-ovarianism, and is a frequent cause of sterility.

DR. ROBERT D. MUSSEY, Rochester, Minn.—The dosage of the different preparations of desiccated thyroid varies. For example, the Burroughs Wellcome product, an excellent preparation, has about one-fifth the strength per grain of the standard products, such as that of Parke, Davis' or Armour's. Often when a paper is discussed it is simply stated that 3 to 5 grains a day are given, while in another a dose of 1½ grains per day is mentioned. We must take into consideration the thyroid product which is being used.

DR. JEAN PAUL PRATT, Detroit, Mich.—Proof that the tubes are closed is sometimes difficult. I am sure we have all had experience with patients becoming pregnant after salpingography showed that the tubes were closed as in one instance noted by Dr. Nicodemus. On the other hand, I have come to feel that the results of the test for the patency of the tubes from above are more or less final. Nevertheless, a patient of mine married nine years had the patency of the tubes tested and at the same time an attempt was made to run salt solution through them. Some five years after that attempt, the patient did become pregnant.

DR. NICODEMUS (closing).—Dr. Rubin's point is well taken about the high incidence of normal sperm in the males. We questioned it very much ourselves and discussed it at length with our very competent urologist. The urologist states that he does the sperm count very accurately and he was not willing to change his mind about the fertility of these husbands.

THE MANAGEMENT OF ABRUPTIO PLACENTAE*

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AT THE present time there is much controversy among obstetricians as to the ideal treatment of abruptio placentae. Holmes[1] and Bartholomew[2] have always been opposed to routine cesarean section. The modified Rotunda treatment was introduced to American obstetricians by Polak,[3] Irving,[4] and Heffernan.[5] The opposite view was given in a paper by Miller[6] before this Society in 1941. Falls[7] also favors immediate cesarean section in the severe cases. In a series of 88 severe cases, Cosgrove and Conway[8] reported a maternal mortality of 4 per cent in those having sections and of 5.26 per cent in those who did not have sections.

The ever increasing number of hospitals with blood and plasma banks should markedly lower mortality from this condition regardless of whether treatment is radical or conservative. Reports of good results of the modified Rotunda method do not mean that these cases should be or can be treated in the home. The ideal place is in the modern maternity unit with an available blood or plasma bank.

In considering the treatment of all degrees of abruptio, it is apparent that individualization is necessary. Much depends upon the severity of the symptoms, parity of the patient, condition of the cervix, whether or not the baby is alive or jeopardized by asphyxia, and whether or not the patient is in labor. It seems better to classify cases according to the severity of maternal symptoms rather than to attempt a pathological classification, which is impossible to demonstrate at the time treatment must be inaugurated. I have studied the cases of abruptio placentae occurring in the last ten years at the Coleman Hospital and the Indianapolis City Hospital. (Fig. 1.) These have been divided into mild, moderate, and severe as has been suggested by McCord[9] and others. The 30 cases occurring at the Coleman Hospital and the 24 at City Hospital are the basis for this paper. At the City Hospital, there were 24 abruptio placentae in 7,497 deliveries, and at Coleman, there was 30 cases in 10,705 deliveries, or a total of 54 in 18,202 cases, or an incidence of one in 337 cases. The incidence of severe cases was one in 2,250.

The Mild Cases

The degree of abruptio may range from a small separation as evidenced by a small clot on the maternal placental surface to the com-

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plete abruptio causing death of the fetus. Some cases of complete abruptio may produce no maternal symptoms. We may have a toxic patient, whom we have attempted to carry to viability, report loss of fetal movements without any other signs or symptoms of placental separation. At delivery, one may find that she has had a complete separation. These cases I have classified as mild. Also included are those

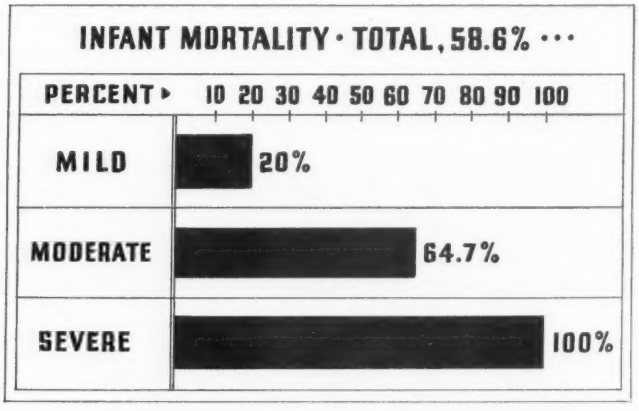

Fig. 1.

cases of slightly increased bleeding during labor with little or no change in fetal heart and requiring no particular treatment. Usually if there is slight separation, labor is so augmented that it is terminated in a short time. These cases then are for the most part cases where the diagnosis is obscure until actual delivery has been completed.

TABLE I. MILD GROUP

CAUSE		TYPE OF DELIVERY	
Toxemia	3	Breech extraction	2
Syphilis	1	Low forceps	4
Trauma	1	Spontaneous	9
Separated during breech extraction	1		

FETAL MORTALITY					
Total cases	15	Stillbirths	2	Neonatal	1

PARITY OF PATIENT		PERIOD OF GESTATION	
Par i	6	7 months	1
Para ii	1	7½ months	2
Para iii	1	8 months	1
Para iv	3	8½ months	1
Para v	2	Term	10
Para vi	2		

In one of my patients, a 40-year-old patient with her first pregnancy, fetal heart tones and movements disappeared about two weeks before term. There was no evidence of toxemia. At the time of delivery, the placenta was found completely sheared from its attachment to the uterus by the presence of white infarcts completely covering the maternal surface. Two years later with a second pregnancy, I did a

cesarean section about 3 weeks from term in the hope of forestalling a similar incident. This time a live baby was obtained, but the placenta showed no tendency to infarct formation.

In this group of 15 mild cases, trauma was responsible for one, syphilis was present in another, toxemia in three, while in the others there was no demonstrable cause except that one placenta separated during a breech extraction.

Only one patient required transfusion. In one case the membranes were ruptured artificially. There were two breech extractions, four low forceps, and the remainder delivered spontaneously. Cesarean section was not used in any case.

Prematurity was present in one-third of the cases evidently caused by the abruptio. There were two stillborn babies and one neonatal death in the series of 15 cases.

In this group interference is almost always unnecessary, and the chief importance is the fetal loss due to prematurity and asphyxia, and the danger of a more severe type of abruptio developing.

The Moderate Cases

This group included those cases where a definite diagnosis could be made during labor. There was usually external bleeding, but shock was not present. In the majority of the patients, the fetal heart was still present. It is in this group where fetal salvage is often still possible. Fortunately, in many of the cases labor has started and is completed in a short time. Some of them will be first seen in the second stage of labor and, if the fetal heart is failing, can be terminated by low forceps. In the primipara just starting labor, cesarean section has its greatest use as the patient is in good condition and the baby can usually be saved. The administration of oxygen to the mother is very beneficial to a failing fetal heart while preparing for operation.

In the 19 cases of moderate severity at the Coleman Hospital, three cesarean sections were done and in each case living babies obtained. In the 12 cases at the City Hospital, sections were done on two patients with a salvage of one baby. Table II shows type of delivery and fetal salvage of the 31 cases of moderate severity. Toxemia was associated in 10 of the 31 cases. Twenty of the 31 were premature labors. Twelve cases required transfusions.

The Severe Cases

In this group, I have placed those patients entering the hospital in shock, with boardlike abdomens and no fetal heart tones. Also I have included one case not in shock, but with entirely concealed hemorrhage and who proved to have a Couvelaire uterus at operation. As this was the mildest of the severe cases clinically, all uteri in the group could be expected to show a comparable amount of damage.

TABLE II. THE MODERATE CASES

	COLEMAN HOSPITAL	CITY HOSPITAL	TOTAL
Type of Delivery			
Cesarean section	3 (1 case with twins)	2	5
Spontaneous	11 (1 case with twins)	7	18
Breech extraction	2	0	2
Breech extraction plus version and extraction	1 (twins)	0	1
Midforceps	1	1	2
Low forceps	1	1	2
Version and extraction	0	1	1
Fetal Salvage			
Total babies	22	12	34
Lived	9	3	12
Died	13	9	22
No fetal heart tone on admission	4	6	10
(Infant Mortality—64.7)			
Artificial rupture of bag of waters	5	0	5
Bag induction	2	0	2
Cause			
Toxemia	7	3	10
Syphilis	0	2	2
Period of Gestation			
7 months	2	4	6
7½ months	4	0	4
8 months	3	4	7
8½ months	1	2	3
Term	9	2	11
Parity			
Para i	10	2	12
Para ii	3	1	4
Para iii	2	0	2
Para iv	2	1	3
Para v	0	2	2
Para vi	0	3	3
Para ix	1	0	1
Para xi	1	1	2
Para xii	0	1	1
Para xiii	0	1	1

These are the patients where the greatest difference of opinion exists as to proper treatment. As the attending staff physician decided the particular treatment of these cases, some have been treated radically and some conservatively, while in one case at the Coleman Hospital, treated under my supervision, treatment was combined.

Unlike many cases of complete rupture of the uterus, when blood is lost faster than it can be given, it is possible to get the majority of cases of severe abruptio into better condition by preoperative transfusion. Therefore, there can be but little argument against waiting until that is done. Instead of procrastination while preparations are being made for transfusion, inauguration of conservative treatment may be attempted in those patients not in labor. The bag of waters

may be ruptured easily in the patient's own bed. I personally prefer not to use a cervical vaginal pack or the bag, and have had no experience with Willett's forceps. A Spanish windlass should be applied and wound tightly, and I believe does better than any type of abdominal binder. A one-minim dose of pituitrin should be given with a tuberculin syringe every half hour for two or three doses.

Fig. 2.—The uterus in the case treated by the combined method.

The question now is (1) whether the uterus can be stimulated to rhythmic contractions so that the baby may be expelled and if so, (2) whether or not the activity of the uterus will be sufficient to control hemorrhage in the early postpartum phase. The obstetrician or a trained resident must constantly observe the patient.

If it is clear that the patient is losing ground in spite of transfusion, as evidenced by frequent blood pressure readings and the character of the pulse, then more blood should be given and cesarean section done. Polak recognized this possibility and one of his 16 patients was so treated. On the other hand, it is remarkable how, in many cases the uterus can be stimulated and active progressive labor will be started. Anyone who has not attempted this method of treatment will be impressed by its advantages, if he will only give it a trial. In some cases the labor will be short, terminate spontaneously, postpartum uterine activity will be satisfactory and after the first 24 hours, the patient

will progress as a normal patient to be discharged much sooner than if she had been operated upon.

In 34 patients treated conservatively, Irving had only one case where the uterus would not expel its contents. Also, he has not seen a case where uterine activity would not control postpartum bleeding. However, O'Regan[10] recently reported 2 deaths from this at the New York

Fig. 3.——Microscopic section showing gross infiltration of the blood and separation of muscle fibers.

Lying-in Hospital. One patient at the Coleman Hospital was saved by blood and hysterectomy. Though the baby was delivered by low forceps after conservative treatment, bleeding continued very profusely after expression of the placenta. The uterus was packed and bleeding continued through the packing, necessitating a hysterectomy. It has been stated that a change from conservative to radical treatment is an obstetrical blunder, but to have persisted with conservative treatment here would have meant disaster. The uterus in this case is shown in Fig. 2, and I believe most of you would term it a typical Couvelaire uterus though not to the degree of many. The appearance of the uterus is not necessarily a good criterion as to its ability to contract. A short time after this case, at St. Vincent's Hospital, I did a cesarean upon a patient with her first pregnancy with partial abruptio, but with fetal heart tones still present. Her uterus was very similar in

appearance to this one, but responded nicely after extraction of the placenta and was not removed. Occasionally, in a uterus left at cesarean section, another operation for its removal may be necessary as illustrated in Frank's[11] case. If one does cesarean section on these cases and removes all uteri that show hemorrhage under the serosa and in the region of the great vessels, then many uteri will be sacrificed unnecessarily. I have seen similar petechiae and subserosal hemorrhages in one case of obstructed labor not associated with abruptio, and in another case with marked dextral rotation of the uterus.

Following are eight short reports on the severe cases of abruptio in this series. Another severe case of abruptio, seen in consultation at the Methodist Hospital, was successfully treated by rupture of the membranes, Spanish windlass, and pituitrin.

Severe Cases Treated by Immediate Cesarean Section

CASE 1.—Mrs. M. B., #3701, aged 37, para xi, with history of syphilis, entered City Hospital August 2, 1937, from outdoor service at 8 months' gestation. There were external bleeding and shock. The abdomen was tense, boardlike, and continuous pain was present. The fetus could not be palpated, and there were no fetal heart tones. Blood pressure was 45/0. The patient was not in labor. She was given a 500 c.c. blood transfusion (hemoglobin #6, 33 per cent and red count 1,600,000), and a cesarean section was done. The placenta was completely separated and the uterus was full of dark clots. Another transfusion was given on the second postoperative day. The patient was discharged on the twenty-second postpartum day. She has had three deliveries from below since.

CASE 2.—Mrs. G. D., C-8 841, aged 20, nullipara, a congenital syphilitic, had been receiving antisyphilitic treatment. She was admitted to the Coleman Hospital October 9, 1935, for treatment of toxemia at about 7 months' gestation. She had a fulminating toxemia, urine was loaded with albumin and casts, and there was blurring of vision. She was scheduled for cesarean section and sterilization on October 11. The previous evening, the patient developed sudden pain, started to bleed profusely, her blood pressure dropped from 174/120 to 110/65. She went into shock and the fetal heart disappeared. She was given a transfusion and cesarean section done. Placenta was entirely separated and a stillborn fetus delivered. Hysterectomy was also done, and the patient was discharged on the sixteenth postoperative day.

CASE 3.—Mrs. E. H., XC-24 504, aged 24, nullipara, and a private patient of one of the staff, had been in Coleman Hospital from August 27, 1938, to September 3, 1938, for treatment of a toxemia. She had greatly improved although showing about 0.4 gram per liter of albumin and blood pressure had returned to normal. On September 17, 1938, she was readmitted to the hospital with a very hard boardlike abdomen and in continuous pain. There was no external bleeding. Fetal heart tones were absent. She was operated on shortly after admission, and a stillborn baby at term was removed. Placenta was adherent to top of fundus, attached only around circumference. Between placenta and uterus was a mass of blood clot and free blood totaling about 1,500

cubic centimeters. There was much gross extravasation of blood into uterine wall and the uterus was copper in color. Uterus was removed. Transfusion was given during operation and later two more transfusions were given. Patient was discharged on the twentieth postpartum day.

Severe Cases Treated Conservatively

CASE 1.—Mrs. E. P., 50 585, aged 35, a para v, at 8 months, was admitted to City Hospital at 9:30 A.M., November 6, 1941. She was in definite shock and in labor. Her skin was cold and clammy, and her pulse fast and thready. There were no fetal heart tones. Blood pressure was 40/0. Abdomen was boardlike, and there was some external bleeding. Sequence of events were: admitted at 9:30 A.M.; at 10:00 A.M. she received 500 c.c. blood plasma and 500 c.c. N.S.; vaginal packing was done and 500 c.c. blood given. She also received morphine sulfate, gr. ¼. At 2:30 P.M. she was repacked and at 4:15 delivered a stillborn boy. Another 500 c.c. of blood were given after delivery and was repeated on Nov. 7, 1941. She was discharged on the tenth postpartum day.

CASE 2.—Mrs. D. J., 109176, aged 30, a para v and 7 months pregnant, had a history of nephritis. She was admitted to the City Hospital on my service at 10:15 P.M., September 30, 1940. She was not in labor, but was in profound shock. Skin was cold and clammy. Blood pressure 90/40. Abdomen was boardlike and there was acute abdominal pain, especially on one side. Some external bleeding was present. The red count was 1,700,000 and hemoglobin, 39 per cent. Sequence of treatment was as follows: admitted 10:15 P.M. Spanish windlass was applied, bag of waters ruptured artificially and one minim of pituitrin given. At 11:00 P.M. she was given 1,000 c.c. of 5 per cent glucose in sterile water. At 11:30 morphine sulfate, gr. ⅙. At 1:00 A.M. 500 c.c. of blood. At 3:00 A.M. morphine sulfate, gr. ⅙. At 9:25 A.M. 500 c.c. blood. At 4:40 P.M. spontaneous breech delivery of a stillborn male. At 4:50 P.M. breech extraction of a stillborn female. On October 2, she received 500 c.c. blood and again on October 10. She was discharged on the twelfth postpartum day.

CASE 3.—Mrs. L. F., aged 26, nullipara, C-11 102, with toxemia, was admitted to the Coleman Hospital at 9:00 P.M., August 12, 1936, in labor and in shock with extreme pallor. Blood pressure 100/80, some external bleeding, uterus tonically contracted and no fetal heart tones present. At 10:00 P.M. intravenous of 1,000 c.c. 10 per cent glucose in sterile water. At 12:15 A.M. 500 c.c. transfusion. At 3:45 A.M. intravenous of 1,000 c.c. glucose in distilled water and also sodium amytal, gr. VIISS. At 4:00 A.M. she delivered spontaneously at which time her blood pressure was 200/136. The stillborn girl was near term. The mother was discharged on the fourteenth postpartum day.

CASE 4.—Mrs. B. D., 205 242, aged 36, para vii, was admitted to City Hospital on August 13, 1942, at 2:00 A.M. She was in labor and in shock. Her skin was cold and clammy, uterus boardlike, blood pressure 72/10. No fetal heart tones were present and there was some external bleeding. Sequence is as follows: admitted 2:00 A.M. At 2:25 A.M. given 500 c.c. plasma. At 3:27 A.M. spontaneous delivery of a stillborn girl and uterus packed. At 5:00 A.M. given 500 c.c. blood, repeated on August 14. The patient was discharged on the tenth postpartum day.

Severe Case With Combined Treatment

Mrs. R. B., XC-48 051, a secundipara at term, was admitted to my service at Coleman Hospital at 1:30 P.M., January 31, 1943. She was bleeding profusely, had severe abdominal pain, but was not in labor. She was in shock with cold, clammy skin and thready pulse. Blood pressure was 100/60 and fetal heart tones were absent. Upon admittance, she was given morphine sulfate, gr. ⅙. At 1:30 P.M. she received 500 c.c. plasma and 500 c.c. blood. Bag of waters was ruptured artificially. At 2:00 P.M. a Spanish windlass was applied and one minim pituitrin given. At 6:15 P.M. she was delivered of a stillborn girl by low forceps and the placenta expressed followed by about 800 c.c. of blood and clots. Five hundred c.c. plasma, 500 c.c. blood, 500 c.c. normal saline with glucose, ergotrate intramuscularly and intravenously were administered. Uterus packed. At 8:00 P.M. she was given 500 c.c. of plasma. At 10:30 P.M. 500 c.c. blood started and hysterectomy done (typical Couvelaire uterus). A total of 2,000 c.c. whole blood and 1,500 c.c. plasma were administered. Mother was discharged on fourteenth postoperative day. Without blood and a change to radical management, this patient could not have been saved.

Summary

The 54 cases of abruptio placentae occurring in 18,202 deliveries have been studied. In the 15 cases of the mild group, interference was almost always unnecessary and their chief importance was the fetal loss due to prematurity and asphyxia.

In the 31 cases of moderate severity with 34 babies, the fetal mortality was 64.7 per cent. Five cesarean sections were done, the remainder being delivered through the normal passages.

Of the eight severe cases, three were treated by immediate cesarean section, four were successfully treated by conservative treatment and one was saved by combined treatment. All babies were dead when treatment was started.

There was no maternal mortality in the total series. Total fetal mortality was 58.6 per cent.

Conclusions

1. The availability of blood and plasma is imperative in the treatment of moderate and severe cases of abruptio placentae.

2. The ideal place for cesarean section is in the abruptio of moderate degree with the patient not in labor or with labor not advanced, and fetal heart tones present.

3. For the severe cases, conservative treatment is in many instances ideal, but not all cases can be thus treated successfully.

4. A trial with conservative treatment in the severe group is favored. An occasional patient will require termination by cesarean section, with or without hysterectomy. In the cases expelling their babies through the normal passages, an occasional patient will require hysterectomy because of postpartum bleeding. Combined treatment should play a definite role in the management of abruptio placentae.

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Discussion

DR. SAMUEL A. COSGROVE, Jersey City, N. J.—Dr. Gustafson presents a thoughtful analysis of 54 consecutive cases of abruption of varying degree, managed by different methods, over a ten-year period, without maternal loss. It is doubtful if this splendid record can be generally maintained. Our own last 51 cases also showed no maternal mortality. But in larger series, it is inevitable that there will be some maternal loss due to concomitant factors. In three of the four maternal deaths reported by Conway and myself in 1941, severe toxemia was the sole or importantly contributory cause of death.

I thoroughly concur with the essayist in the following points: (1) The importance of modern resources for blood replacement in successful management; (2) the necessity for classifying and individualizing cases; (3) the validity of the seriousness of maternal symptoms as a basis for classification and estimation of severity; (4) the general applicability of conservative treatment of those cases falling within Dr. Gustafson's mild group, and a large majority of his moderate group; (5) the importance of cesarean section for fetal salvage, and in anticipation of progress to more severe states, in some cases of his moderate group; (6) the extremely rare necessity for sacrifice of the uterus.

Classification of these cases is somewhat difficult. In our former report, we divided cases into only two groups, the mild and severe, in conformity with Dr. Gustafson's own proposal to base such classification on maternal symptomatology. Certainly on this basis some of the cases classified by him as moderate might be considered severe, even though not conforming to the very strict criteria for his severe group. Without such correspondence of classification, it is exceedingly difficult to compare accurately differences in management. However, in regard to those cases which Dr. Gustafson classes as severe, and many of his moderate group, we would be inclined, I think, to place somewhat stronger emphasis than he has on the propriety of radical measures, implemented, of course, by proper antishock treatment.

In our 51 recent cases, there were 38 classifiable as moderate, and 13 as severe, by Dr. Gustafson's scheme of classification. None were of his clinically negligible "mild" type. Of the 38 moderate cases there were:

Cesarean sections	16	42.1%
Delivery by other methods	22	57.9%
Maternal mortality	0	
Fetal mortality	4	10.5%

Of the 13 severe cases there were:

Cesarean sections	10	76.1%
Delivery by other methods	3	23.9%
Maternal mortality	0	
Fetal mortality	13	100.0%

Of the total there were:

Cesarean sections	26	51.0%
Delivery by other methods	25	49.0%
Maternal mortality	0	
Fetal mortality	17	33.3%

Thus, the broader application of radical methods to this group has been salutory to the mothers and appears to have resulted in the salvage of two-thirds of the infants as compared to a fetal loss in Dr. Gustafson's series of almost 60 per cent.

DR. LOUIS E. PHANEUF, Boston, Mass.—The service at the Carney Hospital is a combined one having an equal number of beds in gynecology and obstetrics. I have looked up the obstetric records during the seven years preceding January 1, 1944, and found that during this period of time, there had been 4,508 deliveries. Among these, there occurred 38 cases of abruptio placentae, an incidence of 0.84 per cent or 8.4 cases per 1,000 deliveries. These 38 cases were classified as severe in 9, moderate in 13 and mild in 16. The range in parity was from 0 to 8. The ages ranged from 23 to 46 years. Seven of the women had severe pre-eclampsia. The period of gestation varied between 20 weeks and 42 weeks.

The methods of delivery consisted in the following: in rupture of the membranes, cervicovaginal packing and spontaneous delivery in 21 patients; packing and forceps extraction in 3 patients; Voorhees' bag and spontaneous delivery in 2 patients; vaginal hysterotomy and breech extraction in 1 patient; embryotomy in 1 patient, and cesarean section in 10 patients.

In these 38 cases, 37 mothers recovered, and one died, a maternal mortality of 3 per cent. The mother who died was 23 years of age, a gravida 2, para 1, in the thirty-fifth week of her pregnancy. Her prenatal course had been uneventful until she suffered a fall two days before admission. One-half hour before admission, she began to bleed vaginally. She was not in labor, but bleeding profusely, and the fetal heart tones were good. She was delivered of a living child by cesarean section and was at once given fluids intravenously and 600 c.c. of blood. Her uterus contracted well, but two hours and a half after delivery she had a sudden, profuse hemorrhage from which she succumbed despite all the efforts to combat it. This woman's life might have been saved had a hysterectomy been done, but, at the time of delivery, there was no indication for doing it.

The fetal heart tones were not observed on admission in 14 patients, or 36 per cent. In the group of 38 infants, 16, or 42 per cent, survived. Five babies lived from 3 to 12 hours and 17 were stillborn, thus 22 infants, or 58 per cent, perished. Ten of these 22 dead babies, 45 per cent, were premature.

In regard to cesarean section in the severe cases accompanied by uterine apoplexy, the so-called Couvelaire uterus, I have made an observation which has some practical value. If the bladder is separated from the uterus, there is usually found an area in the lower uterine segment which is free from hemorrhagic changes. This area is of such size as to permit the placing of the transverse half-moon incision within it, but it is not large enough to allow a longitudinal incision without encroachment on that part of the uterus involved in the hemorrhagic process, namely, the corpus. A transverse incision within this zone will permit secure uterine closure, and will be frequently responsible for saving the uterus, whereas in the classical cesarean section, the incision being placed in the hemorrhagic corpus, hysterectomy frequently becomes necessary, because of the difficulty of closing such an incision in hemorrhagic and friable tissue.

THE TREATMENT OF URINARY INFECTIONS WITH SULFASUXIDINE (SUCCINYLSULFATHIAZOLE)*

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The Problem

URINARY infections are frequent and often serious complications of gynecological and obstetrical conditions. The etiological agent in the production of such infections may be any one of a variety of microorganisms, but in the majority of them some member of the coliform group of bacilli is the responsible agent. Of this group *Escherichia coli* is the most frequent offender. These facts are especially true with regard to those infections occurring during pregnancy and the puerperium.

By careful attention to eradication of such contributing factors as lesions productive of urinary stasis and distant foci of infection, much progress has been made in the prevention and treatment of these infections. The therapy of the infections, once established, has been greatly augmented by modern chemotherapeutic methods, especially the use of the sulfonamide drugs. Chemotherapy, however, has proved generally more effective in the acute forms of urinary infections than in the chronic varieties. So long as such complicating factors as stasis or calculus are permitted to exist, even the most efficient means of chemotherapy will usually fail to eradicate the infection. In some other cases, even though no such factors have existed, or if they have existed have been thoroughly eradicated, infection will persist in a chronic state in spite of the most efficient known methods of chemotherapy. In other cases, it is found that the infection will subside temporarily in response to chemotherapy, but will quickly recur after withdrawal of the drugs. Such chronic or frequently recurring infections generally result in slowly progressive damage to the kidneys, and furthermore, constitute an additional hazard, in that should such stasis-producing factors as the physiological dilatation of the renal pelves and ureters occurring during pregnancy or postoperative or postpartum urinary retention intervene, acute febrile episodes of pyelonephritis are very apt to result. It is most important, therefore, that use be made of every available means to accomplish complete and permanent eradication of urinary infections of this type.

Urinary infection by all types of organisms is generally considered to be secondary, in that the organisms reach the urinary tract from

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some source elsewhere in the body. The possible routes by which access to the urinary organs is attained have for many years been the subject of much contention, and a vast literature has grown out of these discussions. The question is not entirely settled, and for the present discussion it is of no great importance. It has been thoroughly reviewed in most textbooks of urology as well as in many independent articles.

For coccal infections, elimination of the source depends upon a thorough search for, and eradication when found, of focal infections in distant parts of the body. In the case of coliform infections, however, the normal flora of the intestinal tract constitutes a permanent massive reservoir of the offending organisms. If this reservoir can in some way be depleted even temporarily, and the constant source of infection thus removed, the normally high resistance of the tissues of the urinary tract to infection may be given a change to recover, so that chronic infection may subside, and frequent recurrences will be less apt to occur in the future.

The Drug

Since about 1940, considerable investigation has been carried out in attempts to find a drug of the sulfonamide group locally effective in the intestinal tract. Such work is still in progress and has already met with considerable success. It is desirable that such a drug should be poorly absorbed from the intestine, so that it may remain to exert its effect upon the bacterial flora of the large bowel, and so that possible toxic effects resulting from its absorption into the blood stream may be reduced to a minimum. To date, the most efficient drug fulfilling these criteria is Succinylsulfathiazole, manufactured by Sharp and Dohme under the trade name of Sulfasuxidine, and first thoroughly studied both experimentally and clinically by Poth and his collaborators[1-4] in the surgical department of the Johns Hopkins University. The chief clinical uses of the drug so far reported are preparation of the bowel for operation upon it, the treatment of bacillary dysentery, and the treatment of ulcerative colitis. Although Poth's first preliminary report appeared in October, 1941,[1] already a considerable literature regarding the use of the drug for these purposes has appeared.

In dogs the drug was found to be nontoxic and harmless when administered in doses of 1 Gm. per kilogram of body weight daily for as long as five weeks. This dosage resulted in a fecal content of the drug of 5 to 10 per cent, and only about 5 per cent of the ingested drug was excreted in the urine. Crystalluria did not occur, and the observed blood levels were never more than 1.5 mg. per cent of sulfathiazole and 2 mg. per cent of succinylsulfathiazole. The dosage for human beings recommended by Poth and his associates was an initial dose of 0.25 Gm. per kilogram of body weight, and 0.25 Gm. per kilogram in six divided doses daily thereafter. With this dosage, the blood level of free sulfathiazole reported by Poth rarely exceeded 1.5 mg. per cent, although

occasionally, higher levels were found for one or two days during the administration of the drug. The highest level recorded was 2.9 mg. per cent, and this was for only one day. The average of 77 determinations in 10 human subjects was 0.95 mg. per cent. The blood levels of succinylsulfathiazole ranged from 0.5 to 8 mg. per cent, the average being 2.11 mg. per cent. In general, the higher blood levels of both substances were obtained on the earlier days of administration following the initial massive dose. The average daily urine excretion in the same cases was found to be 0.34 Gm. of free sulfathiazole and 0.38 Gm. of succinylsulfathiazole.

No toxic reactions to the drug were encountered in the earlier observations of Poth, but subsequently an occasional case with skin rash or febrile reaction has been reported. The subjects in whom these reactions occurred usually have been shown to be highly sensitive to sulfathiazole, as similar reactions were precipitated by single small doses of this drug.[4-6] One case of fatal agranulocytosis following administration of the drug was reported by Johnson.[5] Clay and Pickrell[6] have reported the only case yet recorded of hematuria and crystalluria resulting from administration of the drug.

According to the work of Poth and his associates, the purpose accomplished by this drug is to reduce greatly the concentration of the intestinal bacterial flora, especially the coliform bacilli. It was found that when the suggested dosage was administered the count of *E. coli* in the stools was reduced in from one to seven days from the normal of 10,000,000 or more to less than 1,000 per Gm. of wet stool. In some cases after administration of the drug no *E. coli* could be grown in stool cultures. The drug has the additional effects of overcoming any tendency to constipation and of rendering the stools soft and odorless.

Methods and Results

It occurred to us that in this drug we might have an agent which would be effective therapeutically in the treatment of those cases of *E. coli* infection of the urinary tract which had proved refractory to other means of therapy. To test this supposition, the drug has been used in the treatment of 41 cases of urinary infection. In most of these 0.25 Gm. per kilogram of body weight daily in either four or six divided doses has been given for one week, and half this daily dose for from one to two additional weeks. In 34 of these patients the urine yielded *E. coli* in pure culture. In 17 of these, there was acute pyelitis either during pregnancy or the puerperium, and in the other 17 the infections were not immediately related to the pregnant state.

The character of the urinary infection, the results of previous treatment, and the immediate and remote response to treatment by succinylsulfathiazole, in these 34 patients are recorded in Table I. Disregarding the one patient with calculi in the left kidney in whom a bacteriologic

TABLE I. RESULTS OF TREATMENT WITH SULFASUXIDINE OF 34 CASES OF URINARY TRACT INFECTION IN WHICH PURE CULTURES OF *E. coli* WERE GROWN FROM THE URINE

DIAGNOSIS	CASES	PREVIOUS CHEMOTHERAPY		IMMEDIATE RESULT OF SULFASUXIDINE TREATMENT		LATE RESULTS		
		NO SUCCESS	SUCCESS TEMPORARY	SYMPTOMATIC CURE	BACTERIOLOGIC CURE	NO. FOLLOWED	SYMPTOMATIC CURE	BACTERIOLOGIC CURE
Pyelitis of pregnancy	9	3	–	9	7	9	8	8
Puerperal pyelitis	8	0	–	8	7	7	7	6
Chronic or recurring cystitis	5	–	3	5	5	5	4	3 + 1?*
Acute cystitis	1	–	–	1	1	1	Recurrence 8 mos. with 2nd cure for 5 mos.	
Chronic pyelitis	8	3	1	8	8	5	5	5
Acute pyelitis	2	–	–	2	2	0	–	–
Chronic pyelitis with renal calculi	1	–	–	1	0	–	–	–
Total	34	6	4	34	30	27	24	22

*This patient had always had severe symptoms associated with her recurring attacks of bladder infection. A year after treatment with sulfasuxidine, she reported from England by letter that she had suffered no recurrence of symptoms.

cure was not expected, in 30, or 91 per cent of the 33 patients, the urine was rendered sterile as a result of the treatment. The time required to accomplish this purpose in most of the successful cases was less than one week. Furthermore, in 23 of these patients who have been followed subsequently for from three to twenty months, there has been recurrence of infection in only 3.

Attention is called especially to the 10 cases shown in Table II, in whom previous chemotherapy had proved unsuccessful in so far as any permanent eradication of infection was concerned. It was to determine the effect upon this type of case that the study was originally undertaken, and although the group is small the results have been gratifying, for apparently we have been able to demonstrate in this drug an effective therapeutic agent for a type of case intractable to all previous methods of treatment.

TABLE II. RESULTS OF SULFASUXIDINE THERAPY IN 10 PATIENTS WHO PREVIOUSLY HAD BEEN TREATED UNSUCCESSFULLY OR WITH ONLY BRIEF TEMPORARY SUCCESS WITH OTHER SULFONAMIDES, AMMONIUM MANDELATE, OR BOTH

IMMEDIATE RESULTS		ULTIMATE RESULTS		
SYMPTOMATIC CURE	BACTERIOLOGIC CURE	NO. FOLLOWED	SYMPTOMATIC CURE	BACTERIOLOGIC CURE
10	9	8 2 too recent	8	6

Three of the obstetric patients had been treated previously unsuccessfully with sulfathiazole, one in a previous pregnancy and two in the same pregnancy in which the sulfasuxidine proved successful. Of the nonobstetric group, seven had been treated unsuccessfully with other drugs. In two of these sulfathiazole had been used, in one of them twice, and in a third sulfathiazole, sulfadiazine, and ammonium mandelate had all failed. In four others either sulfadiazine, ammonium mandelate or both had been used with immediate success but had not prevented rapid recurrence of the infection. A few brief case reports will serve better than statistics to emphasize the value of the drug in cases of this type.

CASE 1.—F. L., white, single, aged 58, had suffered an attack of acute left pyelitis in 1938. There had been a febrile course with chills lasting five weeks. Following recovery from this, intravenous pyelography had shown normal excretion of the dye and normal upper urinary tracts. Subsequent to that, she had suffered from attacks of acute cystitis about once each year, each attack lasting about one week, and responding symptomatically to ammonium mandelate administered under the direction of her family physician. She had for years suffered from severe chronic constipation.

She was seen first by one of us (H.S.E.) on July 22, 1942, having just recovered from such an attack of cystitis for which ammonium mandelate had been used. The catheterized urine was microscopically negative, but the culture yielded a heavy growth of *E. coli*. Three days later, July 27, there was recurrence of acute symptoms with massive

pyuria, and again a heavy growth of *E. coli* was obtained. The patient was hospitalized, and 4 Gm. of sulfadiazine were given daily for six days. The symptoms and pyuria cleared rapidly, but the culture was still positive on July 31. On April 6, 1943, there was another flare-up of cystitis with pyuria and *E. coli* bacilluria. Sulfasuxidine 3 Gm. four times daily was begun at once, and continued for one week, and 1.5 Gm. four times daily were given for two additional weeks. On April 13, at the end of the first week, the urine was sterile, the symptoms had subsided, and the patient reported great relief from her chronic state of constipation. There has been no recurrence of symptoms up until the present, and urine cultures obtained on April 20, May 4, June 22, and September 21, 1943, and January 31, and May 27, 1944, have all been sterile.

CASE 2.—R. R., colored, aged 46, was admitted to the gynecological service on August 25, 1941, with acute right-sided pyelonephritis resulting from obstruction of the ureteropelvic junction by a calculus. *E. coli* was grown in pure culture from the urine. The acute symptoms were relieved by nephrostomy and sulfathiazole. On December 30, 1941, cystoscopic study revealed *E. coli* in both the bladder and left kidney urines, and a calculus in the right kidney. The left pyeloureterogram was normal. In march, 1942, she was readmitted and on March 30, the calculus was removed from the right kidney, the lower pole of the kidney was resected, and an incisional hernia which had resulted from the nephrostomy was repaired. Postoperatively she was again given sulfathiazole, but subsequently repeated cultures from the bladder and both kidneys continued to show *E. coli.* On December 2, 1942, sulfasuxidine therapy was started, and a full three-week course was given. After one week of the drug, the bladder culture showed only a light growth of *Staphylococcus albus,* and cultures taken September 23, 1943, January 6, 1944, and June 7, 1944, were all sterile. There has been no recurrence of urologic symptoms.

CASE 3.—T. F., white, aged 19, was delivered June 10, 1942, by classical cesarean section because of severe pre-eclamptic toxemia. The postoperative course was complicated by severe bilateral pyelonephritis, the culture showing *E. coli.* After nine days of sulfathiazole therapy, urine culture still yielded a heavy growth of the organisms. The patient was discharged on June 28, 1942, and readmitted July 2, 1942, with recurrent acute symptoms and a very large tender left kidney. The fever subsided after four days of sulfadiazine, and on the sixth day the urine was reported as sterile, but still contained much pus. On the third admission, July 21, 1942, she again had acute left pyelonephritis with urine showing much pus and a heavy growth of *E. coli.* She was transferred to the gynecologic service where urologic studies showed a left hydronephrosis with obstruction at the ureteropelvic junction. The half hour phenolsulfonphthalein excretion was 10 per cent from the left and 8 per cent from the right kidney.

Ammonium mandelate was given for a week, but the patient continued extremely ill with fever and left flank pain, and on August 8, 1942, the left kidney was explored and removed. The kidney was very large and contained many small cysts suggesting polycystic disease. Many of these were filled with pus, and there was generalized acute pyelonephritis. Ten days after operation, the urine still showed clumps of pus cells and a heavy growth of *E. coli.*

The patient was readmitted September 23, 1942, with recurrent right pyelonephritis due to *E. coli,* and mild uremia. Sulfasuxidine was given for two weeks, the temperature was normal by the sixth day, and the urine from the right kidney was sterile before discharge. There has been no recurrence of acute symptoms. May 31, 1943, the blood nonprotein nitrogen was 53 mg. per cent, the two-hour phenolsulfonphthalein excretion was 25 per cent, and culture of the bladder urine yielded *Staphylococcus aureus.* On March 31, 1943, the urine was sterile, and on January 25, 1944, showed *Staphylococcus albus* and *alpha streptococci.* The last culture obtained on May 18, 1944, was sterile.

CASE 4.—A. B., colored, aged 61, was treated for acute pyelitis and cystitis due to *E. coli* with sulfathiazole for six days beginning April 4, 1943. Culture was sterile on the fourth day of treatment, but was positive again after one month. Urologic studies showed a half hour 'phthalein excretion of 15 and 10 per cent from the right and left kidneys, respectively. The left pyelogram was normal and on the right there was ptosis, hydronephrosis, and hydroureter. Symptoms of acute cystitis and left pyelitis recurred on October 7, 1943. After two weeks of sulfasuxidine, the urine was sterile and microscopically negative. Repeat cultures and specimens six and nine months later, March and June, 1944, were also negative.

CASE 5.—A. M., white, aged 22, was seen first February 10, 1938, at the seventh month of her first pregnancy, having had symptoms of right pyelitis since late December. She had been treated ineffectively with sulfathiazole, which had been tolerated poorly and had caused severe nausea and vomiting. She was running low-grade fever, and the urine contained much pus and showed a heavy growth of *E. coli.* Strangely, she tolerated ammonium mandelate well and was kept afebrile until term by almost continuous use of this drug. The cultures remained positive, however, and whenever the drug was omitted the fever recurred.

After delivery the fever and symptoms subsided. On April 3, 1939, appendectomy was performed for acute appendicitis. Intravenous pyelograms made during convalescence showed normal kidneys and ureters. The bladder culture showed *E. coli,* but the kidney cultures were sterile. Ammonium mandelate was again given, and bladder cultures obtained on June 12, and August 14, were sterile.

A second pregnancy was uncomplicated, and the patient was delivered in November, 1941. She was next seen on January 16, 1943, four and a half months' pregnant with symptoms of mild acute right pyelitis. The urine contained pus, and the culture showed *E. coli.* On January 22, six days after beginning sulfasuxidine, there were no symptoms, and the urine was negative microscopically and on culture. There were no further complications during the pregnancy, but when the patient returned by request on February 28, 1944, the urine showed *E. coli* bacilluria but only an occasional pus cell. Treatment with sulfathalidine 0.1 Gm. per kilogram daily was instituted, and cultures obtained on March 13 and 27, and May 29 were sterile.

CASE 6.—J. B., colored, aged 16, was admitted to the obstetric service on November 2, 1943, at the seventh month of pregnancy, with acute bilateral pyelitis probably of three weeks' duration. The culture yielded

a heavy growth of *E. coli*, and on November 4, sulfathiazole therapy was started with an initial dose of 4 Gm. followed by 1 Gm. every four hours. The patient improved rapidly, and was afebrile by the third day of treatment, but the hemoglobin decreased from 64 to 48 per cent, so the drug was stopped, and a transfusion of 500 c.c. of citrated blood was given. On November 11, she was discharged free from symptoms but the urine still showed 10 pus cells per high power field, and a culture was not obtained. A culture obtained on November 22 was reported as sterile, although the urine contained much pus and the patient was suffering from symptoms of acute cystitis. She was readmitted with recurrent acute pyelitis on December 2, 1943. Sulfasuxidine was started on the day of admission, and all symptoms had subsided by the fourth day, December 5. On December 7, however, there was still much pus in the urine, and the culture was positive. She received 12 Gm. of the drug daily for the first week, and 6 Gm. daily for two additional weeks. She was delivered uneventfully at term on December 28, 1943. Cultures obtained on December 16, December 23, January 1, and February 16 were all sterile. Intravenous pyelograms on January 4 showed normal tracts for the first week post partum.

CASE 7.—R. S. had had a known persistent *E. coli* infection since a hysterotomy in 1934, at the seventh month of pregnancy because of acute pyelitis. There was an acute exacerbation in 1942, treated without specific chemotherapy. She is now pregnant at the date of writing, with the expected date of delivery July 6, 1944. Cultures on December 9, 1943, and January 8, 1944, showed heavy growths of *E. coli*. Sulfasuxidine therapy was begun on the latter date and continued until February 1. On January 18, 1944, the urine culture was sterile and has remained so since. There is a residual urine of about 100 c.c. because of a neurogenic bladder resulting from an old postmeningitic paraplegia.

CASE 8.—C. P., white, aged 39, had had nine pregnancies with only two living children. For seventeen years she had had right flank pain with radiation along the course of the ureter, and recurring pyelitis with each pregnancy. Urologic investigation revealed half hour 'phthalein excretion of 20 per cent from the right and 10 per cent from the left kidney. There was a dense stricture of the left lower ureter with hydroureteronephrosis. The left kidney was removed on June 8, 1942, and showed hydronephrosis and chronic pyelonephritis. Culture from the right kidney just before operation showed *E. coli*. Following the left nephrectomy, the right side was treated by repeated ureteral dilatations and showed cultures consistently positive for *E. coli*. Sulfasuxidine was started on September 21, 1943, and the culture showed a light growth at the end of the first week and was sterile after the second week, and subsequent cultures have been repeatedly sterile. The last one was obtained on June 7, 1944. A hysterotomy and tubal sterilization was done on November 18, 1943, at the fifth month of pregnancy.

Comment

These cases serve to emphasize at least three valuable assets of the drug. Most important of all, the drug has proved effective in eradicating infections which had proved resistant to other forms of chemotherapy including sulfathiazole and sulfadiazine (Cases 1 to 5 inclu-

sive). In Cases 7 and 8, chronic infections which had existed for years and given rise to serious obstetric complications were eradicated. No specific data are obtainable from the records of these two patients as to previous chemotherapy, but the history of both of them indicates a type of infection, which in our experience, has usually not responded well to other methods.

The drug was tolerated well by Cases 3 and 5 who had suffered severe gastrointestinal symptoms from other sulfonamides, and by Case 6 in whom sulfathiazole had produced a rapidly progressive anemia. The renal function in Cases 3 and 8, as well as in several others of the study, especially the one with bilateral renal calculi, was greatly impaired. Nevertheless, the drug was well tolerated by these patients, and only beneficial effects resulted from its administration.

From these observations we may conclude that eradication of the majority of infections due to *E. coli* may be expected from administration of the drug, and that it may be administered without fear of unfavorable reactions even in the presence of severe anemia or marked impairment of renal function.

Many of the obstetric patients with acute infections might have responded equally well to other sulfonamide drugs. However, the role of intestinal stasis in the production of pyelitis of pregnancy has been repeatedly stressed by those interested in the subject. This fact together with the low toxicity of the drug seemed to us to indicate its probable superiority for this type of infection.

In addition to patients with pure cultures of *E. coli* in the urine, seven patients showing cultures of other organisms have been treated. In five of these *E. coli* was also present. The other organism was *Aerobacter aerogenes* in two, *alpha Streptococcus fecalis* in one, and *Staphylococcus albus* in one, and both *Shigella dispar* and *Shigella paradysenteriae* in the other. The patient with *E. coli* and *Staphylococcus albus,* previously unsuccessfully treated with sulfathiazole, was cured and has remained well for fifteen months, suggesting that the *Staphylococcus albus* was probably a contaminant. The treatment was a complete failure in the patient with cultures of *E. coli* and *Shigella.* In the other three, there was symptomatic improvement, and the *E. coli* was eliminated, but the other organisms persisted. A sixth patient with *A. aerogenes* in pure culture was improved symptomatically, but the organism persisted in the urine. In the seventh, the cultures showed *Staphylococcus albus* and *alpha Streptococcus fecalis,* and no beneficial effect resulted from the treatment.

Discussion

We can only speculate as to the mode of action of the drug in accomplishing the results set forth. Alyea,[7] Cook,[8] and others have shown that large doses and high urine concentrations of the sulfonamide drugs

are not necessary in the treatment of urinary infections, and the average daily dose of sulfathiazole or sulfadiazine suggested by these authors is 1.5 to 2 grams. It might be argued from this that even the small

TABLE III. CONCENTRATION IN MG. PER 100 C.C. OF SULFATHIAZOLE IN THE BLOOD AND URINE OF PATIENTS RECEIVING SUCCINYLSULFATHIAZOLE

Blood	0	0	0	trace	0	0	0	trace	1
Urine	12	1.75	–	–	–	4.7	7.6	–	–

amount of free sulfathiazole present in the blood and urine as a result of administration of sulfasuxidine may be the active agent in rendering the urine sterile. This argument seems untenable, however, in view of the very small amounts of sulfathiazole found in the blood and urine of those patients upon whom such determinations were made (Table III), and in view of the fact that several patients were successfully treated with this drug, whose infections had failed to respond to relatively large doses of sulfathiazole.

The only other alternative would seem to be that the tissues of the urinary tract are given an opportunity to rid themselves of the existing infection because the constant source of infection in the bowel is temporarily eliminated.

The reason for persistence of cure, in at least some of those patients who had previously exhibited chronicity or rapid recurrence of infection in spite of other forms of sulfonamide therapy, seems even more difficult to explain. Three possible explanations may be suggested:

First, elimination of the source of infection from the bowel for a period of three weeks may give the tissues of the urinary tract time to recover sufficient natural resistance to infection to protect them against recurrence.

Second, the beneficial effect exerted by the drug upon the intestinal tract may decrease the avenues for escape of organisms into the blood stream or lymphatic channels through which they may have been reaching the urinary tract.

Third, there may be certain strains of *E. coli* with a selective affinity for the urinary tract which are completely and permanently eradicated as a result of administration of the drug.

It seems probable that either the first or second of these mechanisms, or perhaps both of them, may be the explanation for the persistence of cure. It is for this reason that it has been considered advisable to continue the drug for at least two and preferably three weeks. In the majority of those patients cured, the cultures became sterile in less than a week after administration of the drug was begun, so that such an extended course was not necessary to effect an immediate cure.

As regards the third possibility, Meisser and Bumpus[9] long ago demonstrated a selective affinity for the urinary tract upon the part of certain strains of Streptococci. In 1917, Helmholz and Beeler[10] reported a

chance finding which suggested that there may be a similar selective affinity among strains of colon bacilli. Injecting intravenously into rabbits, strains of *B. coli* isolated from the urine of children suffering from pyelocystitis, these authors produced renal lesions in only 8, or 12 per cent, of 66 animals, and the tendency of the organisms to produce lesions in other organs was just as great as in the kidney. In similar experiments using a strain of *B. coli communior* isolated from the urine of a rabbit with a severe spontaneous urinary infection, pyelonephritis was produced in 22, or 70 per cent, of 32 rabbits, and only three of these showed lesions outside the urinary tracts. No other similar contributions have been found in the literature, however, and from discussion of the problem with several expert bacteriologists, we have gained the impression that little is known of specificity of strains of the colon flora, and that any attempt to settle this question experimentally would be met with insurmountable difficulties.

The chief objection to the drug is the large dosage required and the consequent expense to patients of small means. At the present time there is being subjected to clinical trial another drug, phthalylsulfathiazole (sulfathalidine), which from experimental results it is hoped will accomplish the same purpose in daily doses of no more than 0.1 Gm. per kilogram of body weight. We are investigating this drug at the present time, but as yet have not had sufficient experience with it to permit of sound evaluation.

Conclusions

Succinylsulfathiazole has been found effective in the treatment of urinary infections due to *E. coli.*

When administered in daily doses of 0.25 Gm. per kilogram of body weight, the urine is usually rendered sterile in less than one week.

Continuation of the drug in daily doses of 0.125 Gm. per kilogram of body weight for two more weeks seems to protect the patient against recurrence of infection.

The drug has proved effective against infections which had proved resistant to other sulfonamides and to mandelic acid.

The drug is not effective against infections due to organisms other than E. coli.

Because of its scant absorption and low toxicity, it is well tolerated by patients with impaired renal function, or severe anemia who would tolerate other sulfonamides poorly.

Theories of the possible mode of action of the drug are discussed. The most probable mode of action seems to be that elimination of the source of infection from the bowel permits the tissues of the urinary tract to throw off infection by means of their own resistant powers.

The large quantity of succinylsulfathiazole used in this study was made available through the courtesy of Dr. W. A. Feirer of Sharp and Dohme.

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Discussion

DR. FRANKLIN L. PAYNE, Philadelphia, Pa.—As we review the titles of the papers that have been presented before this body during the past few years, we are struck by the scarcity of topics in female urology. It was the teaching of Dr. Clark and of Dr. Keene, my preceptors at the University of Pennsylvania, that female urology constitutes an indispensable part of the gynecologic specialty. I subscribe to this teaching. Therefore, it is particularly pleasing to me to be granted the opportunity to discuss this work that has been done so ably by a gynecologist.

Having had no personal experience with the use of succinylsulfathiazole in the treatment of urinary tract infections, my discussion consists of certain observations that are based upon a review of the literature, including Dr. Everett's manuscript and a limited experience in the management of urinary tract infections by other measures. As Cook stated recently, in simple uncomplicated infections of the urinary tract almost any of the sulfonamide compounds are effective in more than 90 per cent of the cases. We can state further that most acute uncomplicated urinary tract infections clear up within a short time whether treated by means of alkalinization, acidification, alternation of the two, the older so-called urinary antiseptics, simple water diuresis, or by sulfonamides.

The few who do not respond and those with the tendency to recur, such as the ten cases referred to in Dr. Everett's Table II, offer a real opportunity for clinical investigation. His originality in thought and his success in the treatment of the *E. Coli* infections deserve commendation. It is unfortunate that a greater number of the recurrent or intractable cases do not result from this organism. Our experience indicates that *E. Coli* infections occur far less frequently than do those from other types of invaders, which appear not to respond to succinylsulfathiazole.

In the experimental investigation of succinylsulfathiazole, this drug has been shown not to remain entirely within the intestinal canal. Welch, by administering 5 milligrams per kg. per day of each drug to monkeys by gavage, found the average concentration in the blood of succinylsulfathiazole to be 3 mg. per cent, and of sulfathiazole to be 0.8 mg. per cent. Apparently, the latter is formed by hydrolysis.

Poth detected an average of 2 mg. per cent of succinylsulfathiazole and 0.95 mg. per cent of sulfathiazole in the blood stream, following his routine dosage in the human being. While such concentrations are desirable in the treatment of urinary tract infections, by the same token, they may be distinctly harmful to the patient. Poth, Clay and Pickrell, and Johnson have reported a total of four unfavorable constitutional reactions to succinylsulfathiazole—one of which was fatal. These reactions were ascribed to either sensitivity or idiosyncrasy to sulfathiazole and emphasis was laid upon the danger of prolonged administration or intermittent application of sulfonamide therapy. Each of those writers recognized that the ingestion of succinylsulfathiazole is attended by the risk of an untoward response.

Patients who receive this drug—as is true of all sulfonamides—should be kept under careful observation, for it cannot be administered without fear of unfavorable reactions.

In considering the mode of action of succinylsulfathiazole, the essayist pictures the most likely effect to be that of alimentary bacterial depletion with subsequent or concomitant assertion of the natural resistant and recuperative powers of the urinary tract. The chronology of events gives reason to question this conclusion. Poth found that the intestinal flora is about depleted in 93 per cent of the cases at the end of a week. Of 41 cases treated by Everett, 91 per cent of the urines were rendered sterile—usually in less than a week. It is doubtful, that this round the corner therapy could produce simultaneous results in both the intestinal and the urinary tracts, if the latter result is dependent upon completion of the former. The time relationship suggests a dual action, and this suggestion is supported by investigative studies. Poth found the urinary excretion of sulfathiazole to average 0.34 mg. per cent, and that of succinylsulfathiazole to average 0.38 per cent following his routine dosage. Everett found the urinary concentration of sulfathiazole to vary from 1.75 mg. per cent to 12 mg. per cent. He did not report the urinary concentration of succinylsulfathiazole. The remarkable susceptibility of *B. coli* organisms in the intestinal canal to this type of therapy has been demonstrated repeatedly and these organisms should react similarly in the urinary tract. Many writers have emphasized the low dosage requirements in other forms of sulfonamide therapy for urinary infections. It seems reasonable, therefore, that Dr. Everett's results are due first, to local action of these drugs as they are excreted by the kidneys and second, to intestinal bacterial depletion.

DR. J. MASON HUNDLEY, JR., Baltimore, Md.—For many years considerable interest has been centered upon the subject of urinary antiseptics, initiated in some measure by the work of Shohl and Janney[1] in 1917, who showed that the growth of *Escherichia coli* was inhibited by changing the hydrogen-ion concentration of the urine. Some years later Clark[2] and Helmholtz introduced the ketogenic diet, its essential factor being the high fat content in relation to the carbohydrate component. Due to the incomplete metabolism of the fats, a condition of acidosis is produced with the outpouring of ketone bodies in the urine, chiefly beta-hydroxybutyric acid. It has been shown by Fuller[3] that it is this ketone body in the presence of markedly acid urine that produces the desired bactericidal effect. This diet, as will be remembered, was difficult to carry out as it frequently produced severe gastrointestinal disturbances.

Another advance was the introduction of mandelic acid. This substance, which is secreted unchanged, is efficacious only in a markedly acid urine, the acidity being accomplished by the administration of ammonium chloride. Ammonium mandelate, as it is now produced, is of use in patients in whom sulfa therapy is not tolerated and continues to be used in selected cases.

No real success was attained, however, in the treatment of urinary tract infections until the introduction of sulfanilamide and its closely related substances. The most popular urinary antiseptics today, I believe, are sulfathiazole, sulfadiazine and sulfamerazine, and probably the latter evokes fewer untoward reactions than any of its associated compounds. As is well known, after continued use of the sulfanilamides, organisms originally susceptible may become fast and the drug be ineffective. The use of sulfasuxidine for persistent urinary tract infections, particularly those due to the *Escherichia coli*, seems to be a distinct advance and well worthy of trial. In this relation I have had no personal experience, having employed it only with intestinal operations and especially in the preoperative treatment of complete perineal lacerations.

Sulfasuxidine therapy will be of inestimable value in treating pyelitis with pregnancy when the usual infecting *Escherichia coli* is not susceptible to the sulfa group.

In using any type of chemotherapy for urinary infections, it is first obligatory to relieve any obstructive lesion. If such a condition is not removed, there is no permanency of urinary sterilization, for with cessation of therapy there is soon a return of the infection.

I agree with the essayist that permanent cures are difficult to explain when they are initiated by only a temporary sterilization of the bowel content, this being complete or more frequently incomplete.

When one reviews some of the opinions in regard to the lymphatic relationship between the bladder and kidney and especially between the large bowel and kidney, it is more difficult to understand how a permanent cure could be produced. Franke[4] has demonstrated that lymphatics from the large intestine pass over the capsule of the kidney, that the kidney has a rich network of lymphatics that emerge at the hilum, and that there is a connection between these lymphatics and those of the capsule. Mayer[5] is of the opinion that the lymphatic connection only occurs between the colon and the right kidney and that pathologic changes of the intestinal wall are necessary before a transmigration of organisms can take place, probably explaining, if he is correct, the intermittency of kidney infections. Regardless of these anatomic findings, which may not be constant, sulfasuxidine would appear to be of great value in eradicating persistent urinary infections due to the *Escherichia coli*.*

DR. EVERETT (closing).—Dr. Payne spoke of the possible dual action of this drug, and he is quite right in emphasizing this point. I emphasized the mode of action through the intestinal tract particularly because some of these cases had not completely cleared up with the administration of sulfathiazole alone. It is possible that the two modes of action together may be the final answer, but I do believe that the elimination or reduction of the intestinal flora is at least partly responsible for the results obtained.

Dr. Hundley stressed the eradication of urinary obstructions, and I have mentioned that point in the paper also. Our clinic under the leadership of Dr. Hunner has for years stressed the importance of establishing adequate renal drainage in the treatment of infections as well as many other diseases of the urinary tracts. Every possible effort was made to eliminate any discoverable obstructive lesion in each of these cases.

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MATERNITY CARE IN THE UNITED STATES—PLANNING FOR THE FUTURE*

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MY REMARKS this evening will be devoted to the consideration of the development of a nationwide maternity service.

The object of this Society, as stated in its constitution 68 years ago, was the promotion of knowledge in *all* that relates to obstetrics, the diseases of women, and abdominal surgery. The distinguished fellows of the Society and its guests have presented and discussed in the annual meetings many of the great clinical advances made in obstetrics and gynecology during this long period. Rarely, however, do the transactions of the Society reveal any discussion of the ways and means whereby the great knowledge and skills developed in these specialties could best be made available to the greatest possible number of women in the United States.

Dr. Taussig in his presidential address of 1937, "The Story of Prenatal Care," spoke as follows of Dr. Ballantyne: "The dawn of the twentieth century found his spirit rising with the hope of an age when all expectant mothers would be properly cared for."

In the presidential address of Dr. Holden in 1939, and of Dr. Litzenberg in 1941, significant statements were made. Dr. Holden said, "We can no longer retire to our clinics and laboratories but must take our proper place in all broad programs of social welfare which affect the health of our people" and Dr. Litzenberg stated, "Medicine certainly cannot attain its proper place in society by resisting all of the impacts of social change."

Advances in the science of obstetrics have been truly great during the history of this society. Have methods of making available and applying this knowledge of maternity care on a nationwide basis been given sufficient consideration?

I was first requested to speak on obstetric care in wartime, but later broadened the title since wartime measures must be considered in relation to what has gone before and what may occur in the future.

Twenty-five years ago, there were but practically few specialists in obstetrics. Most women were delivered by the family doctor or kindly neighbor women. Today, a growing number of women in the United States recognize the better care provided by physicians specially trained in obstetrics, and the demand for maternity care by specialists is rapidly increasing.

*Read, by invitation, at the Sixty-Eighth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 19 to 21, 1944.

Graduate education and experience definitely planned to train specialists in obstetrics, or obstetrics and gynecology, have developed within the lifetime of many of you here. Before the second World War, not more than 2,500 physicians limited their practice to this specialty, and less than three-fourths of these were Diplomates of the American Board of Obstetrics and Gynecology. More than two million, or 4 out of 5, maternity patients in 1912 did not receive the expert care which a specialist in this field can give. One basic guide for future planning should be the following principle:

> That in the United States *all* maternity patients should have advice and treatment throughout the maternity cycle by or under the immediate supervision of a doctor of medicine recognized as a specialist in obstetrics.

Eight years ago only two-fifths of all births in the United States occurred in hospitals. More than two-thirds of the births now occur in hospitals. Although 84 per cent of maternity patients in urban areas obtained hospital care in 1942, only 45 per cent of those in rural areas were cared for in hospitals. What plans should be made for providing hospital maternity care for the million women now unable to secure such care each year? In planning for the future, a second basic guide should be the following principle:

> That *all* maternity patients should have care during labor and during at least the first 10 days after delivery in hospitals equipped and staffed to provide all possible safeguards to the health of mother and infant, and all maternity patients with serious complications during pregnancy should have care in such hospitals.

How can the objectives stated in these two principles be attained? There would appear to be three major steps:

1. Training the additional obstetricians needed.
2. Building the additional hospital facilities needed.
3. Developing a plan which will assure the effective utilization of such specialists and facilities in providing care for all maternity patients without regard to their economic status.

Training Additional Obstetricians Needed

Theoretically, all obstetric care and teaching in the United States could be provided by approximately 10,000 specialists in obstetrics, including the resident obstetricians in training, if the obstetricians and hospital facilities needed were geographically so located as to be accessible for 2,500,000 maternity patients each year. This estimate is calculated on the premise that all births would be occurring in hospitals, with one obstetrician or resident obstetrician in training for approximately every 250 maternity cases each year. (Since students

and interns, under supervision, would deliver many women in the teaching hospitals, the number of patients actually attended by the senior teaching staff would be considerably less than the figure of 250 used in this calculation.)

In 1942, approximately 2,500 physicians limited their practice to obstetrics or obstetrics and gynecology. The American Board of Obstetrics and Gynecology had examined and certified as specialists less than three-fourths of these physicians. At least 7,500 additional fully qualified obstetricians are needed in the United States and a plan should be made for their training. This number could be trained in 10 to 15 years after the war.

Table I shows the number of additional obstetricians needed in each State.* The 439 hospitals in which 1,200 or more births occur each year have a total of approximately 720,000 births each year. If all hospitals reporting 1,200 or more births a year could meet necessary standards of approval for the 3-year training of residents in obstetrics

TABLE I. NUMBER OF ADDITIONAL OBSTETRICIANS NEEDED IN EACH STATE TO PROVIDE ONE OBSTETRICIAN FOR EVERY 250 LIVE BIRTHS

Alabama	262	Nebraska	76
Arizona	28	Nevada	11
Arkansas	164	New Hampshire	37
California	390	New Jersey	254
Colorado	71	New Mexico	54
Connecticut	10	New York	422
Delaware	15	North Carolina	324
District of Columbia	4	North Dakota	43
Florida	128	Ohio	446
Georgia	259	Oklahoma	155
Idaho	45	Oregon	72
Illinois	432	Pennsylvania	586
Indiana	267	Rhode Island	42
Iowa	168	South Carolina	182
Kansas	118	South Dakota	48
Kentucky	246	Tennessee	230
Louisiana	199	Texas	501
Maine	62	Utah	55
Maryland	105	Vermont	27
Massachusetts	210	Virginia	237
Michigan	407	Washington	117
Minnesota	180	West Virginia	162
Mississippi	220	Wisconsin	229
Missouri	191	Wyoming	21
Montana	41		

or obstetrics and gynecology, and if for approximately every 1,200 births occurring annually, they would graduate each year one resident completing 3 years' training, there would soon be an annual increase of approximately 600 in the number of obstetric specialists. When such a training program was fully operating, each teaching hospital would have a first-year, a second-year, and a third-year resident in training for each 1,200 births, or a total of approximately 1,800 residents in training.

*In addition to number of physicians limiting their practice to this specialty at time of Procurement and Assignment survey in 1942.

There should be no difficulty in obtaining this number of residents immediately after the war when thousands of young physicians with little or no previous opportunity for graduate training will be released from military service. The continuing supply of approximately 600 residents in training to be appointed each year would be approximately 10 per cent of the number of physicians completing internships each year before the war. The 600 physicians completing their 3-year resident training each year would provide the additional specialists needed until some 10,000 qualified obstetricians were available. After this quota was reached, about 300 new specialists would need to be trained each year for replacements due to death or retirement.

If obstetrics and gynecology were combined in the service of the specialists under discussion, and it is believed that they should be, some modification would be necessary in the estimated number of specialists and hospital beds required.

Building Additional Hospital Facilities Needed

Approximately 30,000 additional beds are needed to provide hospital care for all the maternity patients now delivered at home. Table II shows the number of additional beds needed for each State. Some of the beds should be in maternity units of general hospitals which should be constructed for the most part in small communities, and others would probably be in 20- to 40-bed maternity hospitals to be constructed in rural areas where the establishment of a general hospital would not be practicable. Under Government postwar building programs to absorb manpower released by the Armed Forces and war

TABLE II. NUMBER OF ADDITIONAL HOSPITAL MATERNITY BEDS NEEDED IN EACH STATE TO PROVIDE HOSPITAL CARE FOR ALL DELIVERIES NOW OCCURRING AT HOME

Alabama	1,849	Nebraska	259
Arizona	125	Nevada	9
Arkansas	1,143	New Hampshire	46
California	453	New Jersey	296
Colorado	239	New Mexico	313
Connecticut	56	New York	710
Delaware	48	North Carolina	2,060
District of Columbia	55	North Dakota	126
Florida	673	Ohio	1,316
Georgia	1,599	Oklahoma	763
Idaho	81	Oregon	55
Illinois	875	Pennsylvania	1,903
Indiana	843	Rhode Island	67
Iowa	502	South Carolina	1,268
Kansas	375	South Dakota	141
Kentucky	1,785	Tennessee	1,497
Louisiana	1,025	Texas	2,380
Maine	212	Utah	102
Maryland	530	Vermont	78
Massachusetts	256	Virginia	1,389
Michigan	956	Washington	79
Minnesota	454	West Virginia	1,103
Mississippi	1,648	Wisconsin	527
Missouri	1,059	Wyoming	38
Montana	47		

industry, the construction or expansion of hospitals to provide this number of additional maternity beds would be possible over a period of 10 years and would cost on an average approximately $15,000,000 during each year of construction, probably with larger expenditures in the earlier years of the period. This cost is estimated on the basis of $5,000 per bed. The location of additional hospitals should be determined on the basis of need in relation to the number of maternity beds in existing hospitals, the number of births in given areas, and the transportation problems involved. Ambulance service (automobile and possibly airplane) should be affiliated with the hospitals in some areas.

Every hospital should have proper facilities for obstetricians on the staff to provide prenatal care for all the patients living near enough to come to the hospital for this purpose. The time and energy of physicians would be conserved if they had their offices in the hospital where all their patients received hospital care. Patients would be more likely to receive all the laboratory, x-ray, and other special diagnostic services needed if these were available in the same building in which they received office care. In some of the less populated areas, maternity patients should be able to receive prenatal care in health centers near their homes, the obstetricians on the staff of a near-by hospital treating patients in such health centers perhaps one day each week. The smallest maternity unit of a general hospital or small maternity hospital should have at least 20 beds, which would provide accommodations for between 500 and 600 maternity cases per year. Twenty maternity beds would serve a population of approximately 25,000, and two obstetricians could provide all maternity care for most areas with this population. Maternity units serving sparsely populated areas might need to have accommodations near by where women living long distances from the hospitals could be housed for a week or more before the expected date of confinement.

In order to provide hospital maternity facilities wherever needed, Federal grants should be made available for their construction. These grants should be made only when the new hospital or enlargement of existing facilities are in accordance with a State-wide plan of the official State health agency for hospital facilities—which had been made after a thorough survey of the needs of the State and which would assure the most effective utilization of such facilities. The architect's plan and the standards of construction should, of course, meet recognized modern standards for satisfactory maternity units.

Some of the Present Conditions Affecting Future Planning

Eight years ago in the programs initiated under the Social Security Act, provisions were made for the extension and improvement of health services for mothers and children throughout the United States. Since that time, the State and local health agencies have greatly increased health education in this field, established clinics for prenatal and in-

fant care, employed thousands of public health nurses, who as a part of their duties, advise and assist women in the prenatal and postpartum periods, established and enforced higher standards of hospital maternity services, provided postgraduate training in obstetrics for thousands of physicians, public health nurses, and hospital nurses, and initiated and carried out many studies of maternal morbidity and mortality. Approximately $10,000,000 is now expended each year under this nationwide maternal and child health program; and these services have undoubtedly been in part responsible for the decrease of more than 50 per cent in maternal mortality rates during these 8 years.

Insurance for loss of wages during unemployment and to provide income during old age has been firmly established under the Social Security Act and now covers more than 40,000,000 people, or one-third of the entire population of the United States.

Voluntary insurance for hospital care began approximately 10 years ago, and now provides protection for between 15 and 20 million people in the United States. Approximately one-fourth of all hospital care provided under Blue Cross insurance plans is for maternity care. Medical-service plans and group health insurance cover the cost of medical care on a prepayment basis for more than 3,000,000 people today. Under the Michigan Medical Service plan, for example, obstetric and gynecologic services represent 36 per cent of the total cost of all service provided. The protection afforded by unemployment, old age, and health insurance is thoroughly appreciated by most American families.

It appears likely that next decade will see a rapid expansion in prepayment or taxation plans for financing the costs of medical and hospital care. Whether such plans will ultimately be financed on a voluntary basis similar to Blue Cross, or by compulsory pay roll deduction, general taxation, or combinations of these, is uncertain. Present trends indicate that the method of paying for medical care is rapidly changing from the variable individual expenditure to new bases which more equitably distribute the cost.

The extent to which Government is now directly concerned with provisions for maternity care is significant. About 15 per cent of all births now occur in Government hospitals and the cost of most of this care is paid from tax funds. State and local public agencies arrange and pay for the care of many other maternity patients in nongovernmental hospitals. The emergency maternity and infant care program, established as a wartime service, is providing care this year for approximately 15 per cent of all maternity cases. It may be conservatively estimated that between one-fourth and one-third of all maternity cases in the United States are now having their care paid for from public funds.

A few words concerning the EMIC program. Fifteen months after war was declared, when it became obvious that thousands of the wives of the enlisted men needed help in planning and financing their maternity care, the Congress made funds available to the State health agencies, through the Children's Bureau, to provide medical, nursing, and hospital maternity and infant care as a matter of right for the wives and infants of enlisted men in the four lowest pay grades of the Armed Forces.

This program as developed and administered is on the whole quite satisfactory to the patients and their families, to hospitals, and to the general practitioners who at present provide most of the maternity care in the United States. Many specialists in obstetrics, however, feel that the rates of payment for maternity care under the program should have been more in line with their usual charges for private patients rather than based upon the usual charge of general practitioners. When the program started, the Children's Bureau suggested a differential rate of payment between specialists and general practitioners, but the physicians on the Advisory Committee of the Children's Bureau recommended no differential in the rates. This month 20 obstetricians, most of them in private practice, met with the Children's Bureau and again expressed the opinion that it would be very difficult to work out a practicable method of establishing different rates of payment to the general practitioner and to the specialist.*

In many communities the specialists in obstetrics have not fully realized the valuable service they could render under this program by assisting the State agencies in arranging as far as possible for the general practitioners to call them for consultation and help with complicated cases. The preparation of lists of the best-qualified consultants in various areas of each State has been most difficult, and in only a few States have the obstetricians actually assisted the State health departments in selecting the best-qualified men for such lists. The question of requiring obstetric consultation, where available, when serious complications occur, should be receiving more consideration. If the specialists in obstetrics were being called by general practitioners when serious complications occur, not only would there be better care of the individual patient, but there would also be an improvement in the quality of maternity care by general practitioners as a result of the educational value of consultation.

The administrative framework and policies for the EMIC program were, of necessity, drafted and applied to fit a temporary nationwide program which had to be put into operation in as short a time as possible. Since many of the individuals eligible for care were moving

*Since this article was submitted for publication the Children's Bureau of the Department of Labor has amended its policies for the administration of the EMIC program to provide, *at the option of each State agency*, differential rates of payment to specialists for care confined to their specialty if the rates do not exceed by more than 50 percent the maximum rates adopted by the State agency for general practitioners and do not exceed the rates customarily paid to such specialists.

from State to State, and many physicians and hospitals near State lines provided care for patients from 2 or more States, policies of administration had to be reasonably uniform between States. No comparable program had been undertaken before in this country. Many State health departments had little or no experience in the administration of public medical-care programs. It is really quite remarkable that, at the end of the first year, care was being authorized under the program for more than 40,000 new patients each month and in all States and Territories and it appears now that care for between 15 and 20 per cent of all maternity cases in the United States will be provided under this program during the next year. The Children's Bureau believes, however, that many of the methods of administration that have, of necessity, been adopted for this emergency wartime program, designed to meet the needs of a selected group of maternity patients, would be unsatisfactory for a more permanent nationwide maternity service.

Many individuals have asked to what extent Government will be concerned with provisions for maternity care after the close of the war when authorization for the EMIC program will have expired. No one can predict what the sentiment of the people will be—and it is they who will determine what responsibility Government will have in this field. Fortunately, the EMIC program has provoked and will continue to provoke much discussion concerning the best method of providing and financing maternity care.

Planning of national health programs to meet the needs of citizens over the world is widespread at the present time. In the United States labor, farm, and other citizens' groups, Federal, State, and local governmental agencies, and several State or local medical societies are proposing or experimenting with a variety of tax-supported or insurance plans. Organized medicine has made it clear what it does *not* want, but has left everyone uncertain as to what it does want. A realistic attitude on the part of the practicing physicians toward changes which are taking place and intelligent leadership in the medical profession for planning for the future are needed urgently.

The problem of how to pay for medical or hospital maternity care now confronts more than 2½ million families throughout the United States each year. For many of these families the cost of maternity care is a major economic problem. Studies show that in 1942, when war industry was rapidly expanding, 62 per cent of the families of two or more individuals in the United States had money incomes of less than $2,500 a year. Less than 10 per cent of such families had money incomes of $5,000 or more a year. In the peacetime years of 1935 to 1936, 85 per cent of such families had incomes of less than $2,500 and only 3 per cent of the families had incomes of $5,000 or more. Few of these families under present methods of financing can pay the cost of high quality medical and hospital care. Yet all these

families should receive needed care by physicians specially trained in obstetrics, and this care should be given in modern maternity hospital facilities. Methods of providing the best possible maternity care to all families living in the more than 3,000 counties of the United States must be studied.

If the additional specialists and hospital facilities needed, as outlined in the early part of this paper, are made available, what type of plan would be most likely to assure their effective utilization in providing good maternity care in all parts of the United States? Good maternity care for all families of the United States cannot be assured if we depend upon the ability of a few to pay the costs on the sliding scale of fee for service and the present haphazard efforts to provide care for those unable to pay.

The cost of providing all the maternity care needed in the United States should be determined and sound plans for financing and provision of such services should be agreed upon.

A careful estimate indicates that the total annual cost of providing medical and hospital care for all maternity cases could be in the neighborhood of $250,000,000. Included in this amount is an estimate of the total net income of 10,000 obstetricians at a beginning rate of $2,000 net per year for first-year residents and a maximum of $20,000 net per year for chief obstetricians in the largest teaching centers. Also included is the total cost of hospital care for all maternity patients, as well as maintenance of physicians' offices in the hospitals and all laboratory or other diagnostic and consultation services. The $250,000,000 is equivalent to 60 cents per month for each family in the United States.

Obstetricians will not be accessible to all maternity patients until these physicians are assured adequate income irrespective of the ability of the community to provide it. Residents might be appointed under an agreement to practice in a hospital in a smaller community for at least 5 years after completing their training. Remuneration of physicians must be commensurate with the training and experience of the individuals, the responsibilities of their positions, and the quality of services provided.

If a nationwide plan for maternity care, financed entirely from the revenues of general taxation or from insurance contributions supplemented by tax funds, were to be adopted, some of the principles of administration which should be observed may be outlined briefly as follows:

Administration should be primarily a local community responsibility and the hospitals of the future should become the community centers for all preventive and curative services. Physicians participating in the service in any community could determine whether they wished to be paid on a case basis or a salary basis. I believe that the appointment by hospitals of full-time obstetricians to provide care for all

maternity patients seeking care at the hospital or its affiliated health centers will ultimately be found to be most satisfactory for all concerned. Patients should have free choice among the obstetricians and hospitals accessible to them.

Minimum qualifications required for the appointment of obstetricians to hospital staffs would have to be established, and within 10 or 12 years, it could be required that all obstetricians on hospital staffs have the training and experience required of Diplomates of the American Board of Obstetrics and Gynecology. Until a sufficient number of obstetricians were trained, there would be many communities in which maternity care could be provided only by the general practitioners now including obstetrics in their practice. The responsibility for the maintenance of a high quality of medical and hospital service for all hospitals in a region, for consultation, and for periodic review of cases in the medium-sized or smaller hospitals should be placed on the staffs of the medical school and other teaching hospitals with which all other hospitals in the region with maternity services should be directly affiliated. All specialists should have opportunity each year to keep fully informed on advances in this field of medicine and to have readily available all the diagnostic and treatment facilities that may be needed for the best possible care of maternity patients.

To assure maintenance of the hospital maternity services in any community, regardless of its economic status, the hospitals must be freed from their dependence upon contributions or upon the overcharging of private patients to make up for the loss through free services. Any approved hospital should be paid from public funds on a cost basis for providing all in-patient maternity care and care for newborn infants and the cost of maintenance of facilities for prenatal care and all laboratory, x-ray, and other special diagnostic services for maternity patients. Payments from public funds for hospital care should be dependent upon (1) the hospital's maintenance of established standards of equipment and services, (2) upon agreements to provide within the limits of their accommodations, maternity care for any woman applying for such care, irrespective of her residence, race, or economic status, and (3) upon the affiliation within a region of all maternity services from the first-line university and teaching hospital centers through medium-sized hospital maternity services to the smallest hospital or maternity-home, in order that consultation, diagnosis, and other services of the larger hospitals might be made as readily available as possible to the smaller hospitals.

Medical and hospital maternity care should be supplemented by education of the public—through the work of the public health nurses and through the press, radio, and other media—regarding the need for and value of good maternity and infant care. The public should be given instruction, too, as to the proper diet and hygiene for the mother during the maternity cycle, and for her baby, and how such a diet can be

obtained within the resources of the ordinary family. Also, household-aid services should be established in all communities to provide help when needed in the home during the hospital confinement and convalescence of the mother.

If a nationwide plan for comprehensive health services for the whole population were adopted, the program for maternity service here outlined would become a part of a national health program.

I am confident that the ways and means will be found for assuring all expectant mothers the best possible maternity care. This objective cannot be attained without proposing plans, studying them carefully, and modifying them as necessary, until they are acceptable to the citizens receiving care as well as to the professions providing care.

The suggestions in this paper are those of the author. The Children's Bureau before committing itself to any definite policy will continue to study and review with its advisory groups the many problems relating to extending and improving health services for mothers and children in the United States.

Discussion

DR. JOHN R. FRASER, MONTREAL, CANADA.—It has been a great privilege to hear one who is so conversant with obstetric conditions outline what he feels should be the future plan to control the management of pregnant women in the United States.

There are two fundamental principles which govern this scheme: first, that all pregnant women in the future shall be under the control and management of an obstetric specialist; and, second, that all obstetric patients shall be hospitalized. Of course, that is an all-embracing and most important statement, but to put it into effect is another matter. I thought Dr. Daily's suggestion excellent, that one of the first things should be a three-year training of men who are considering life as an obstetric specialist. That is naturally important as the general surgeon has already determined so well. The statement that 84 per cent of pregnant women today in urban localities are hospitalized and only 45 per cent in the rural communities is of interest to me. In Canada, 47 per cent only of our pregnant women are hospitalized and this is one of the basic obstacles to the whole scheme. In the sparsely settled areas, it will be very difficult, at least for a long time, to bring about any hospitalization scheme, desirable as it may be.

I would like to discuss this problem from the angle of our Canadian situation because we are in the midst of formulating what I think is a very important scheme. In certain parts of Canada, for instance in Alberta, they have taken a step which is extreme in one direction, for they have set aside $700,000 so that pregnant women shall receive treatment free. Across the country we come to the opposite extreme where Quebec gives us 34 cents a day for the mother and the same amount for the baby. That is all the State offers to one who cannot afford hospitalization. To correct this great divergence in planning, the Canadian Government has before Parliament a Health Insurance Act which has been formulated, I am glad to say, in association with organized medicine. The profession has participated from the very beginning and, while we have not been able to direct it by any means, we have been able to follow along with it and give advice.

Every person in the country, 16 years of age and over, will be taxed $9.50 per annum which will provide for medical care of all descriptions, including a complete obstetric service. We believe that will provide a fund of something like a

hundred and seventy odd millions, and it is hoped that the obstetric patient will share generously in that fund.

From all these insurance schemes, there has arisen a special problem for the teaching hospital, namely, that the more we assist and provide for the obstetric patient the less material we are to have for instructing our students. We are already having much more difficulty getting teaching material and it has been definitely written in this new Bill that any patient receiving public funds shall be considered to be a patient upon whom teaching may take place. This is a fundamental question because we have found already with any of these insurance schemes that it has encouraged a feeling on the part of the patient against being used for teaching purposes. As the Labor Party announced in Parliament, "We do not propose to be guinea pigs any longer."

In conclusion I would like to remind you that the United States government by a policy of education and by the efforts of agencies in Washington and allied associations has been able throughout the country in the last 15 or 20 years definitely to lower the mortality rate. The same process has been seen in Canada. Before adopting any scheme that may be formulated, we must bear in mind that we should maintain what we have at present and not upset that important doctor-patient relationship which is fundamental in medicine. We should also remember that the system we have at the present time has not done too badly.

DR. FRED L. ADAIR, CHESTERTON, IND.—In approaching a discussion of this subject, we ought to begin with a consideration of some very important fundamental principles which are involved in our ideals of democracy. There are certain things that we have to accept in a democratic form of government and among these are equal opportunities for every citizen insofar as it is possible to supply these. Two basic requirements in securing these equal opportunities are education and health. These two basic ideas are very closely tied one with the other. My remarks will be mostly confined to the basic principles of health.

We have to look at a maternity and infancy program not as a program in itself, but as one which is definitely tied in with all health activities. In developing a maternity and infancy program it should be integrated with other health as well as educational activities.

Now one of the principles of democratic government which I believe is fundamental for all governmental activities is local self-government. Federal taxation, or even State taxation, has certain important objectives. One of these is to pay the necessary expenditures of governmental activities. The other is to provide funds for the equalization of essential activities in various communities. Any federal funds which are appropriated should be viewed from these two angles, one to pay the necessary expenditures of the federal government; the other to distribute these funds so that under local self-government these funds can be, as nearly as possible, equalized for the attainment of these objectives which I have mentioned.

If large proportions of these funds appropriated by federal and state governments could be used for hospitals and equipment for the practice of modern medicine, we could gradually evolve a system which would preserve the individuality of the medical profession, and, at the same time, provide through these facilities, improved opportunities for practice by the medical profession. This would result in the type of service which we would like to have every mother in the country receive. I do not know how the organization of such a plan can be worked out except by evolution, and by the trial and error method. It is quite possible that the same method may not apply to different areas.

With reference to hospitals, it seems to me that there should be first a relatively simple setup which would be adequate for the care of the more ordinary medical problems, including maternity cases. There should be in addition institutions for providing more specialist care in larger areas so that it could be possible to shift

patients from communities where relatively simple care was enjoyed, into areas where much more highly specialized care could be supplied.

In brief, this represents my viewpoint. We must work out a health program with reference to maternal and infancy care which is in accordance with our democratic ideals.

DR. NICHOLSON J. EASTMAN, BALTIMORE, MD.—Quite obviously Dr. Daily's paper raises a number of issues, controversial issues it is true, but living issues and issues of the utmost importance to all of us. Three questions which it raises seem to be deserving of our particular consideration, as follows: (1) What will be the

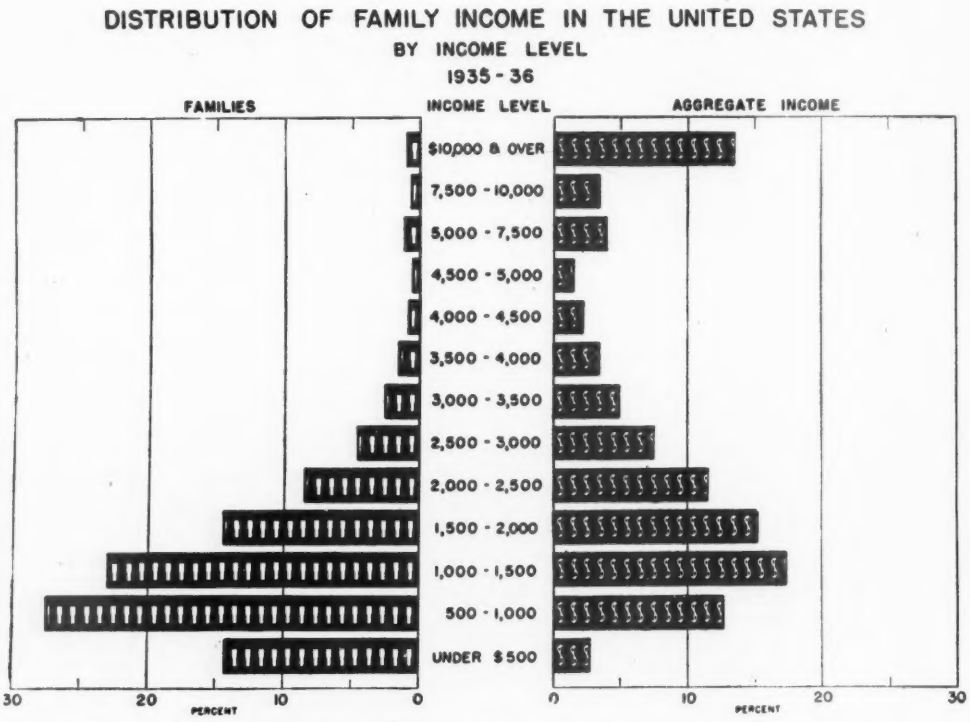

Fig. 1.—This chart may be read either by length of bars or by symbols. Each figure symbol represents 1 per cent of all families or 294,000 families. Each dollar symbol represents 1 per cent of aggregate income of all families or $476,792,380.

effect of this program which he visualizes on the quality of maternity and infant care in the United States? (2) What will be the effect of this program on the private practice of obstetrics? (3) And what will be its effect on the individual initiative and enterprise of obstetric specialists?

Fig. 1 shows, as of 1935 to 1936, the percentage of families which fall into the various income groups: 1 per cent having $10,000 or over, and so on down. It can be concluded from these statistics that some 41 per cent of our families in 1935 to 1936 received incomes of $1,000 or under. I think that everyone here will agree that such a level of income is not adequate to pay for the best obstetric care with its increasing complexities.

Yet, that is not all. Those who are acquainted with such matters tell us that people in these lower income brackets have illnesses and require the attention of doctors with twice the frequency of those in the upper income brackets, and we all know that the birth rate is much higher in these lower income groups. Ac-

cordingly, while we may say that some 40 per cent of the families in 1935 to 1936 had income levels under $1,000, this group required much more than 40 per cent of the total obstetric and medical care needed by the nation. What has happened to these people in the past? They have been taken care of, for the most part, by county, state and federal funds, but it is well to recall that a large number of them have not been taken care of at all.

Fig. 2.

Fig. 2 shows that in many of the southern states over 80 per cent of the Negro births occur without benefit of medical attention. It is instructive to note that in these very same states in which so many Negro births are without benefit of medical care, that the maternal mortality is the highest. This of course may be a coincidence, but there is valid evidence indicating that a relationship exists between

the fact that so many people in these lower income brackets receive no medical care at delivery, and the higher maternal mortality rate.

It is my feeling that the plan recommended by Dr. Daily would go far toward improving obstetric care in these areas and among those groups who do not have adequate income to provide for private obstetric care; and, by the same token, it should improve maternal and infant mortality rates the country over.

What effect would this plan have on private practice? I would direct your attention to the right side of Fig. 1. While it is true that families with incomes of $10,000 and over represent only 1 per cent of the families of the United States, they received 13 per cent of the aggregate income. It can be deduced further from these statistics that the families, who have an income of $2,500 and over, receive some 30 per cent of the aggregate income. Now these families with incomes of $2,500 and over, who receive one-third of the total income available in this country, are the ones who have heretofore supported the private practice of obstetrics, and I cannot see why such a scheme as Dr. Daily's, directed at this lower income bracket, should affect private practice among upper income groups, who will doubtless want to continue with private practitioners.

Finally, let us consider the effect of this plan on individual enterprise and initiative. What rewards will this plan offer to the young man who is contemplating obstetrics and gynecology as a specialty? What rewards for intelligence, industry, originality of thought, research, surgical skill and executive ability? Any such scheme must provide such rewards, not only financial but academic rewards, for otherwise, our better young men will not be interested in entering the specialty. Of course, if that should happen, the program would be a toboggan which would carry us back to medieval midwifery. But I think that a plan can be worked out which does offer rewards to stimulate individual initiative.

The Society is to be congratulated on being able to hear this contribution of Dr. Daily. It is a subject which we must not get angry about, for it is a matter that deserves our dispassionate consideration. Surely, it is our responsibility to think very clearly about this whole problem and make certain that we reach conclusions that serve the best interests of both the mothers of our country and our specialty.

DR. EDWARD A. SCHUMANN, PHILADELPHIA, PA.—Am I correctly under the impression that this Society is, consciously or unconsciously, engaged in a discussion of socialized medicine, or partly socialized medicine? If so, I must suggest that the matter is of such importance that it cannot be determined in a few hours. If it is the will of the Society that we should discuss the matter, it should be made the basis of an important symposium by the entire Society.

DR. CARL HENRY DAVIS, WILMINGTON, DEL.—I think I am one of the few who has had an opportunity to see something of medicine as it is practiced where all care is given by the government. I had the opportunity of visiting Russia in 1934 and 1935 when they were lessening the obstetric problem there by doing thousands of abortions every month. However, this was stopped in about 1936, and when I was there in 1937, the medical service of the government was having great difficulty in expanding its facilities rapidly enough to care for all pregnant women. Moscow was visited three times and I attempted to learn as much as possible about their medical practice. Their entire medical plan seemed to be worked out much like our teaching clinics. It is undoubtedly true that the average Russian receives much better medical care than he did formerly.

In the completely socialized state the doctor has a favored position. Professor Yudin, one of their foremost surgeons, received a salary of 25,000 rubles, which was many times the income of the average worker. He was on duty at the hospital a

specified period each day for five days and then he had a full day off. Free time was supposed to be used for research and study as well as recreation. This plan might have an appeal to those of us who have no control of our time.

Dr. Daily's plan to train 10,000 capable obstetricians would require many years and if patients demanded the services of individual men it might be impossible. One of our difficulties since the plan for the care of servicemen's wives has been the lack of hospital service cases for delivery by our interns.

Experience in large clinics suggests, however, that a considerable part of the population is interested in good service rather than the services of a certain doctor. It is my belief that obstetric care could be made less personal by having two or more men work together in such a way that only one would need to be on duty at the hospital during a night. The great mass of patients cannot pay for the type of services we as specialists try to furnish. Most of us could deliver several times as many patients each year if our deliveries could be accomplished in a manner which would lessen the number of disturbed nights. Skilled obstetric service for all will require radical changes from our present personal type of service. I think some plan should be worked out so that patients on a minimum pay basis could be delivered by an intern and have the obstetrician take care of them if there were complications.

DR. DAILY (closing).—The major purpose of presenting this paper was in order to bring to your attention what is really a serious problem today, and one which I think will confront us much more in the future. I hope all of you will be giving it a great deal of thought and attention. We should decide upon the objectives that we want; the methods of obtaining them are of secondary importance. If we can agree that we do want the best maternity care that can be provided in this country, for all mothers, I am sure that we can achieve it.

Department of Reviews and Abstracts

Review of New Books

Gynecology

Everett's Gynecological and Obstetrical Urology[1] is a single volume treatise devoted exclusively to urology of the female. At the Johns Hopkins Hospital, Howard Kelly's pioneer work with his direct vision cystoscope in the air-dilated bladder, and Hunner's observations on ureteral stricture and the elusive ulcer have influenced this school and are emphasized in this volume. The direct method of cystoscopy, which rarely is taught or used in other schools, is described in detail. This was the first method of cystoscopy that I learned, and although I now rarely use it, I can vouch, personally, to the simplicity and applicability of the direct method, but find that patients object to the posture. The various renal function tests are described. The indications for both intravenous and retrograde urography are outlined. For the excretory method, diodrast or neoiopex are recommended.

The cause of nongonorrheal chronic urethritis is ascribed to distant focal infections such as endocervicitis, trigonitis and ureteral stricture. The author emphasizes that with the advent of chemotherapy, the local treatment of cystitis by irrigation and instillation has decreased almost to the vanishing point. A very detailed description of interstitial cystitis—the "elusive" ulcer of Hunner—is given. Resection of the bladder for this lesion, has been abandoned; instead, strong topical applications are made to the small affected areas. Description of postradiation disturbances and lesions of the bladder is given. Vaginal cystotomy still is advocated for removal of vesical calculi which cannot be extracted through the cystoscope or cannot be crushed. The operation for simple stress incontinence consists of reefing the tissues at the bladder neck (Kelly's technique). In my experience, it is not possible to find adequate structures for this repair in every case as shown in Fig. 83 of the author. The treatment of vesical fistula, as well as that of ureteral fistula, is adequate. The various techniques for transplantation of the ureters into the bowel are described, including rectal implantation by the vaginal route.

Succeeding chapters deal with lesions of the kidney and ureter. Nephropexy for movable kidney producing symptoms is indicated in only about one-fourth of the patients. Ureteral stricture and multiform effects ascribed to it are detailed. The clinical forms of renal infection, tuberculosis of the urinary tract, calculous disease and tumors and trauma to kidney and ureter are fully described.

This urology of the female is lavishly and artistically illustrated. The reproduction of the x-ray films is unusually good. Chapter bibliographies are judiciously selected. This is a valuable contribution. The gynecologist and obstetri-

[1]**Gynecological and Obstetrical Urology.** By Houston S. Everett, A.B., A.M., M.D., Associate Professor of Gynecology, the Johns Hopkins University and Associate in Gynecology, the University of Maryland. Assistant Visiting Gynecologist and Gynecologist in Charge of the Cystoscopic Clinic, the Johns Hopkins Hospital. Visiting Gynecologist, the Church Home and Hospital, the Hospital for the Women of Maryland and the Union Memorial Hospital. 517 pages. The Williams & Wilkins Company, Baltimore. 1944.

cian heretofore have been forced to wade through books on general urology, which focus chiefly on lesions in the male, in order to find scant references here and there to problems restricted to female patients.

R. T. FRANK.

Dr. Corner, who has previously written a book designed for the laity called the *Hormones in Human Reproduction*, has now written another volume, **Ourselves Unborn. An Embryologist's Essay on Man**[2] which appears as the twenty-first Terry Lecture. Usually a book designed for the laity, with very few exceptions, is an unpleasant chore for the reviewer. This certainly cannot be said for this volume which deals with embryology, particularly with human embryology. Dr. Corner has an uncanny talent for presenting in nontechnical terms the most difficult subjects. In this embryology, he gives the minutiae of this science, based on the huge Carnegie Institute collection, in a fully understandable fashion, and in such a way as to prove as absorbing and worth-while reading to the physician or medical student as to the lay reader. It requires a special talent to accomplish this difficult task. I have no hesitation in recommending this book to the profession as warmly as I do to the inquiring and educated layman.

R. T. FRANK.

A very logical publication arrangement brings two companion volumes on the subject of infertility which together consider the fertility of a couple rather than merely that of an individual. Siegler in his **Fertility in Women**[3] discusses the causes, diagnosis, and treatment of impaired fertility in the female while Hotchkiss in his **Fertility in Men**[4] discusses the same topics with regard to the male in the sterile mating.

In **Fertility in Women**, Siegler develops a logical perspective in his discussion of the subject. In his opening, and somewhat historical chapter, he makes the surprising statement that among Catholics the birth rate fell steadily from four offspring in a marriage in 1913 to two each in a marriage in 1920. Other racial and geographic factors are here evaluated.

The author's evaluation of fertility reveals its complex nature, and he discusses the various types of sterility, with a definite and methodical plan of investigation of sterile matings including the history, physical examination, and the marital relation. Proceeding to physiologic and functional development, there is a comprehensive discussion of the physiology of the female sex cycle. Particularly is this developed in relation to ovulation; the factors producing it, as well as the relation of ovulation to the various phases of the sexual act. Considerable space is devoted to the determination of the time of ovulation. Performances of various tests to determine the functional changes of the menstrual cycle are detailed and illustrated. The author assumes from the many investigations of his own and others that ovulation may occur at any period in the cycle, but particularly from the eighth to twentieth day. He feels that the simple procedures of proved value are sufficient to determine ovulation and may be checked, when necessary, by endometrial biopsy and hormonal assays. In the third part of the book he takes up treatment, discussing the factors and the

[2]**Ourselves Unborn. An Embryologist's Essay on Man.** By George W. Corner. 188 pages. Yale University Press, New Haven. 1944.

[3]**Fertility in Women.** By Samuel L. Siegler, M.D., F.A.C.S. Attending Obstetrician and Gynecologist, Brooklyn Women's Hospital; Attending Gynecologist, Unity Hospital. With a Foreword by Robert L. Dickinson, M.D. 194 illustrations including 40 subjects in full color on 7 plates. J. B. Lippincott Company, Philadelphia, London, and Montreal. 1944.

[4]**Fertility in Men.** By Robert S. Hotchkiss, B.S., M.D. Lieutenant Commander (MC) USNR (on active service), Asst. Prof. of Urology New York University Medical College. With a Foreword by Nicholson J. Eastman, M.D. 95 Illustrations. J. B. Lippincott Company, Philadelphia, London, and Montreal. 1944.

methods which may be used to overcome infertility. He states in this discussion that relief of sterility by hormonal therapy was found to be variable, unpredictable and disappointing. The surgical therapy of conditions accounting for faulty reception of spermatozoa is discussed. It is interesting to note that the author had four, of twenty-three patients operated upon for tubal occlusions, conceive and deliver at term. One feels that the author is opposed to artificial insemination; he states that very few sterile couples qualify for it.

In the companion volume, **Fertility in Men,** Hotchkiss discusses the subject of infertility from the male standpoint. Particularly valuable is the opening chapter regarding past prejudices on the part of the male and suggestions as to the physician's approach to this phase of the question. The author discusses the anatomy and physiology of the male genital organs, and describes the various pathologic lesions which may influence the function of the testes and other elements of the male generative tract.

A comprehensive picture of the metabolism and composition of the semen is given. Under clinical inferences, the author discusses the relationship of the female genital secretions as they are related to the welfare of the sperm. This question is also taken up by Siegler in his book, and apparently this relationship forms one of the still unsolved questions of infertility.

Several succeeding chapters are devoted to the methods of appraising fertility in men, which include laboratory analyses, cell counts and morphology with a discussion of the variabilities of semen and the factors which influence their characteristics.

Dr. Hotchkiss closes this book with a very rational consideration of the problems of treatment, and he has made a final chapter of unusual value by including case histories to illustrate effects of treatment in the deviations of semen, volume, motility, number, percentage of abnormals, usually encountered. The text is clear and concise and emphasis has been placed on the practical details.

These companion volumes are highly recommended to all those who are interested in any part of the subject of infertility since they offer a fine working guide to the problems of a couple so troubled.

PHILIP F. WILLIAMS.

A second edition of **Novak's Textbook of Gynecology**[5] has appeared after an interval of three years. The text has been enlarged by more than one hundred pages, and forty additional illustrations. The title of the book has been shortened from *Gynecology and Female Endocrinology* to a *Textbook of Gynecology.*

The revision has been thorough. Two new chapters have been added. The embryology is largely based on the slides loaned by Dr. Robert Meyer. The description of the formation of the vagina is particularly adequate, and the illustrations are interesting. The final chapter, written by H. S. Everett deals with the common disorders of the female urinary organs. It covers the ground adequately. The treatment of gonorrhea is to be commended because the main treatment now consists of sulfa therapy with entire omission of local treatment during the acute stages. It might have been mentioned that the small number of sulfa resistant cases, particularly the chronic ones, can be cured by means of penicillin.

Throughout the text, Gartner's duct, etc., is "Gärtner's." August Gärtner was a German bacteriologist after whom the Gärtner's bacillus, a member of the salmonella group was named; Herman T. Gartner was a Danish anatomist who described the residue of the Wolffian duct found in the female.

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[5]**Textbook of Gynecology.** By Emil Novak, M.D., F.A.C.S. Associate in Gynecology, The Johns Hopkins Medical School; Gynecologist, Bon Secours and St. Agnes Hospitals, Baltimore. Second Edition. 709 pages. The Williams and Wilkins Company, Baltimore. 1944.

Novak's Gynecology is a very readable textbook which covers the ground thoroughly. The author has the ability to describe conditions clearly and particularly to correlate, clarify and epitomize the enormous amount of material which has accumulated. Short bibliographies are found at the end of each chapter.

R. T. FRANK.

Peel has undertaken the task of revising and enlarging a **Textbook of Gynaecology** by Forsdike.[6] Judged by American standards the book approaches an ample compend rather than a textbook. The chapters on physiology and hormonal control are clear and up to date. The clinical conditions are tersely and well presented. The treatment advised is conservative.

The illustrations of gross specimens are good and numerous. The drawings of microscopic specimens are quite schematic, the photomicrographs are better. An appendix containing "endocrine products available in Great Britain and the Colonies" contains a long list of biologically tested pharmaceuticals with names foreign and unknown in the United States. For the student studying in this country the book has little to offer.

R. T. FRANK.

History of Gynecology by Leonardo[7] has a foreword by Greenhill and a second one by Victor Robinson. The subject is covered in twenty-eight chapters, and takes in the usual history of ancient medicine beginning with the Egyptians and the middle ages, the gynecology of the Renaissance, and those of succeeding centuries.

To me the most interesting chapter is that on recent advances in which the author covers the development of gynecology in the last one hundred and fifty years very briefly, but containing a great deal of worth-while material. The book is well written and makes pleasant reading. There is a bibliography at the conclusion, and both a subject and authors' index which make reference easy.

R. T. FRANK.

The third edition of **Gynecological Therapy** by Calatroni and Ruiz[8] to appear since 1938, is a huge tome of 1212 pages, 38 chapters, with 442 illustrations. It has been brought up to date by incorporating into the text our newer knowledge on sulfa therapy, androgen therapy and discussion of the possible carcinogenic effect of prolonged use of estrogens. A new chapter on nonvenereal skin lesions of the vulva has been contributed by Quiroga. The chapter on neuropsychiatry is by Thenon.

The encyclopedic contents of this volume preclude an attempt at detailed review. Every field of gynecology including the allied gynecologic endocrinology and radiotherapy are covered. Particular attention is given to functional disturbances. Cancer as well as benign lesions are dealt with.

True to the title, therapy is the main theme, described in detail and often embracing remedies, which have been abandoned in this country. Operative tech-

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[6]**Forsdike's Textbook of Gynaecology.** Revised, enlarged and in part rewritten by J. H. Peel, M.A., B.M., B.Ch. (Oxon.), F.R.C.S., M.R.C.O.G., Assistant Obstetric and Gynacological Surgeon, King's College Hospital and Princess Beatrice Hospital, etc. 440 pages. Grune and Stratton, New York. 1944.

[7]**History of Gynecology.** By Richard A. Leonardo, M.D., Ch.M., F.I.C.S. Fellow Royal Society of Medicine (London); Fellow American Medical Association; Fellow International College of Surgeons, etc. Forewords by Prof. J. P. Greenhill (Loyola University) and Prof. Victor Robinson (Temple University). 434 pages. Froben Press, New York. 1944.

[8]**Terapeutica Ginecologica.** Por Carlos J. Calatroni, Docente Libre de Clínica Ginecológica (Buenos Aires), Jefe de Trabajos prácticos de la Cátedra and Vincente Ruiz, Professor Titular de Clínica Ginecológica (La Plata), Docente Libre de Clinica Ginecologica (Buenos Aires) III Edicion. 1212 pages. Ferrari Hnos. Buenos Aires. 1944.

niques are outlined, frequently also illustrated. Each chapter is followed by an ample formulary of prescriptions. Liberal, but on the whole conservative, use of endocrine therapy is advocated. According to the authors no substantiated proof of carcinogenesis in the human being due to the use of estrogens, has been demonstrated. Androgen therapy is limited by its high cost and the dangers of masculinization.

The book is lavishly and effectively illustrated. Due credit is given to authors when their illustrations are used. On the other hand, in this large volume there is no bibliography and no index.

R. T. FRANK.

Proceedings of the Conference on Problems of Human Fertility edited by Engle[9] gives a detailed account of the meeting held in 1943, under the auspices of the National Committee on Maternal Health. Three topics were discussed—criteria of ovulation, some biological observations on the lower generative tract, and in what fashion the placenta acts as a barrier between mother and child. These fundamental questions were dealt with by a number of well-known investigators. It is impossible to single out individual articles for review. The aspects covered were endocrine, embryological, histological, chemical as well as physiological. The material is presented in a very compact way and in each instance followed by a discussion by members of the conference. A huge amount of information is given, information much of which has not yet reached publication.

R. T. FRANK.

Obstetrics

In this historical review **Hydronephrosis and Pyelitis of Pregnancy**[10] Dr. Robertson documents 974 references. The facts and theories presented in these articles and the deductions which he has drawn from them are presented in a series of fourteen chapters, which in discussing the etiology and pathogenesis of the two subjects under consideration brings out the anatomic relations, bacteriology, nervous chemical and nutritional influences. There are also chapters on eclampsia, intravenous urography and the end results of hydronephrosis and pyelitis in pregnancy. He summarizes the material in the chapter entitled "Discussion" after which he enumerates the conclusions which may be drawn from his historical review.

Robertson feels that if the dilatation of the ureter in pregnancy is abnormal enough to constitute a real disease, and this is his attitude, then measures for its prevention as well as avoidance of its more dangerous complications should be instituted. He regards hormonal influences and chemical and nutritional disturbances as minor effects. Infection, pyelitis and pyelonephritis are regarded as subsequent to stasis. The author feels that every inflammation of the renal or urinary pelvis is accompanied by inflammation of the renal substance. He is skeptical about primary pathogenicity of *B. coli*. He argues against the hematogenous route and feels that most inflammatory lesions are due to pathogenic bacteria which regularly inhabit the urogenital regions.

Regarding the prognosis he suggests postpuerperal intravenous urographic studies. Space has not permitted him to discuss the relationship of pyelitis to the fetus,

[9]**Proceedings of The Conference on Problems of Human Fertility.** Sponsored by the National Committee on Maternal Health, January 15 to 16, 1943, New York City. Edited by Earl T. Engle. 182 pages. Published for the National Committee on Maternal Health by George Banta Publishing Company, Menasha, Wisconsin. 1943.

[10]**Hydronephrosis and Pyelitis (Pyelonephritis) of Pregnancy: Etiology and Pathogenesis.** An Historical Review. By H. E. Robertson, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minn. Pp: 310. W. B. Saunders Company, Philadelphia, 1944.

interruption of pregnancy, or immediate life expectancy of the mother. Surgery he states should be undertaken as a last resort, and he advises no succeeding pregnancy if any evidence of infection persists. This review is an excellent recapitulation of the history and present-day facts on these urological entities.

PHILIP F. WILLIAMS.

Weisman and Coates have written a complete monograph on **The South African Frog (Xenopus Laevis) in Pregnancy Diagnosis.**[11] This covers the subject very completely, including the discovery of this animal, its habitat, anatomy, behavior, reproduction, etc. The African frog was first used for pregnancy tests in South Africa, then taken up by Crew of Edinburgh, and introduced into this country by Weisman. Apparently, the frog has been used extensively now by others. As a test object, the accuracy compares with both the original Aschheim-Zondek and the Friedman tests.

To those unfamiliar with this test, it should be mentioned that the same frog, if given a vacation of four weeks, can be used many times. However, according to Weisman's technique, eight frogs which would be sufficient for four tests, require three tanks of twelve gallons each in order to have a stock, a preparatory, and a recovery tank. The authors use, except in advanced pregnancy, a concentration of urine, precipitating 80 c.c. of urine with twice the amount of acetone. The precipitate either obtained by decantation or centrifuged is then allowed to dry and is taken up in 2 c.c. or more of distilled water. An alternative method after precipitation is to filter, and adjusted to a pH of 5.5. The animal is injected in its dorsal lymph space, with the equivalent of 40 c.c. of urine, and then placed in a small test tank containing a one-half inch mesh screen, a small distance from the bottom of the tank, through which the extruded eggs drop. The animals are examined every four hours. If, after eighteen hours, no eggs are visible, the test is considered negative. Animals which react negatively may be used again in three to seven days.

In reading this monograph it becomes apparent that considerable care in keeping these animals is required. Their present cost, at retail, is ten dollars each.

R. T. FRANK.

In **Caesarean Section, The History and Development of the Operation From Earliest Times**[12] which Dr. Young submitted as a graduation thesis of the University of Edinburgh in 1942, one finds a very complete history of this procedure. He has delved deeply into the origin of the name of the operation and its early performances. He divides his story of the development of this operation into three periods: that prior to 1500, the second period from 1500, when the first authenticated operation of cesarean section was performed on a living woman, and the third period from 1876, which year marks the beginning of the development of the modern technique of the operation following the work of Porro and Sanger.

In the first section, the author has reviewed the literature of the time with extensive quotations from the records of those days. It would seem that most of the operations performed in that period were emergencies with high mortality.

[11]**The South African Frog (Xenopus Laevis) in Pregnancy Diagnosis.** A Research Bulletin. By Abner I. Weisman, M.D., Adjunct Gynecologist, Jewish Memorial Hospital; Assistant Visiting Gynecologist and Obstetrician, Metropolitan Hospital, New York, N. Y. and Christopher W. Coates, Aquarist, New York Zoological Society, Research Associate to the Department of Pathology, Jewish Memorial Hospital, New York, N. Y. Aided by a grant from the New York Biologic Research Foundation. 1944.

[12]**Caesarean Section: The History and Development of the Operation From Earliest Times.** By J. H. Young, M.B., Ch.B. Pp:224. H. K. Lewis and Co. Ltd., London, 1944.

In the second period up to the introduction of the Porro operation, the terrible mortality produced a tremendous debate on the relative merits of cesarean section and craniotomy. Nevertheless, as the author shows, the operation was increasingly performed in various countries.

The more successful results obtained by the technique of Porro, led to development of the classical operation and the seroserous approximation of the uterine wound popularized by Sanger. After recounting the ever broadening modern indications for cesarean section, the author relates the efforts to popularize cesarean section in placenta previa. He describes the efforts to avoid infection and in the more recent attempts to reach the uterus extraperitoneally.

The author has given us a fine recital of the origin of this operation and of the stages through which its evolution has come. The work is well documented and the quotations from writings difficult to obtain are usually full. The book should be of interest to those interested in the origin as well as the present place of the operation in obstetric practice.

PHILIP F. WILLIAMS.

The last issue of **Dr. Greenhill's Year Book (1943)**[13] is again replete with a valuable review of the annual progress in this field of medicine. The abstracts from the literature are complete and supplemented by valuable editorial comments as well as a most satisfactory index. The principal topics dealt with include the use of the sulfa group of drugs, caudal anesthesia, vaginal infestations, clinical pelvimetry, progesterone treatment of abortion, androgen therapy, hemorrhagic disease in the newborn, endometrial biopsies, treatment of obstetric hemorrhages, etc. Notwithstanding the absence of references to the foreign literature, there is no apparent reduction in the size of the present volume, which demonstrates the extent of the activity of American authors. Greenhill's work constitutes an invaluable source of information for the practitioner as well as the specialist in obstetrics and gynecology.

GEO. W. KOSMAK.

Dr. Read in his **Childbirth Without Fear**[14] again stresses the significance of emotional factors on the reproductive functions of women to which he first called attention in 1933 in the book *Natural Childbirth.*

He regards pain, fear, and tension as a syndrome which is responsible for the pain of labor, and explains the various factors which predispose to a low threshold of pain interpretation and which may be regarded as subject to correction. In discussing the factor of fear, he analyzes this emotion in relation to mental imagery, and brings out the point that fear of childbirth is becoming a conditioned reflex bringing about the idea of pain and its associated tension.

He feels that a thorough explanation in early pregnancy to the patient of the physiology of parturition and the various phenomenon of labor would do much to dispel the fear factor as a conditioning reflex. He explains thoroughly the type of education employed both in pregnancy and at the beginning of labor, as carried out in his own practice to the point where anesthesia is seldom, if ever, needed. His application of the practice of relaxation in obstetrics, the therapeutic method developed by Jacobson, brings about, apparently, a lessening of the tension factor. He details instruction on the method by which such relaxation may be obtained.

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[13]**The 1943 Year Book of Obstetrics and Gynecology.** By J. P. Greenhill, M.D., Chicago, The Year Book Publishers, Inc. 1944 p. 584. Price, $3.00.

[14]**Childbirth Without Fear. The Principles and Practice of Natural Childbirth.** By Grantly Dick Read, M.A., M.D. Pp: 257. Harper and Brothers. New York and London. 1944.

Since American women have been so sold, by lay publications, on the idea that parturition is an exceedingly painful process, it is to be doubted whether a widespread adoption by obstetricians of Read's technique would bring about childbirth without fear earlier than within a period of several generations.

PHILIP F. WILLIAMS.

Special Delivery by Rosenberg[15] is a handbook for expectant mothers. In a clear, understandable way, the anatomy of the pelvis, the mechanism of labor, the changes in the puerperium, in fact the entire process of delivery, including the anesthesia, forceps, etc., are given. This little manual is well illustrated. Its purpose is to dispel in the most effective way the phobias entertained by pregnant women. Whether even this nicely presented description will actually serve its purpose must be considered doubtful. There is no question that an intelligent, well-poised and well-balanced woman may derive distinct benefit from such knowledge. On the other hand, the fearsome neurasthenic may very well react in quite the opposite way.

R. T. FRANK.

The thirteenth edition of **DeLee's Obstetrics for Nurses**[16] appears under the authorship of M. Edward Davis, M.D., and Mabel C. Carmon, R.N., who have succeeded the late Doctor DeLee. The book has been reorganized on the unit basis to bring it in line with the recommendations of the curriculum guide of schools of nursing. The authors are fortunate to have had the assistance of many able leaders in the obstetric and nursing field in preparing various sections of the book, and the criticisms of those who are actively engaged in obstetric nursing. Specifically, one may mention the excellent new section entitled, "The Reasons for Failure of the Fetus or Young Infant to Survive," which particularly emphasizes the points brought out in an earlier section in the fifth unit in nursing in the neonatal period.

PHILIP F. WILLIAMS.

Thirty Cases of Puerperal Infection by de Carvalho[17] is a brief monograph, detailing thirteen of the case histories. The value and dangers of the sulfa drugs are discussed.

Miscellaneous

In this book, **Pain Mechanisms**[18] Dr. Livingston discusses the clinical aspects of pain, especially the study and interpretation of the clinical syndrome which may develop following nerve injury and which is designated as "causalgia." He acknowledges the complexities of the problems regarding pain, and the difficulty of presenting the results of clinical observations and of physiological investigation in a manner at once acceptable to research workers as well as to the

[15]**Special Delivery. The Expectant Mothers' Handbook.** By B. D. Rosenberg, M.D. With illustrations by Gladys McHugh. 96 pages. Ziff-David Publishing Company, New York. 1944.

[16]**DeLee's Obstetrics for Nurses.** By M. Edward David, M.D., Professor of Obstetrics and Gynecology, University of Chicago and Mabel C. Carmon, R.N., Chief Supervisor and Instructor in the Birthrooms, Chicago Lying-in Hospital and Dispensary. Thirteenth Edition, Reset. Pp: 575. Ill. 306. W. B. Saunders Company, Philadelphia and London, 1944.

[17]**Trinta Casos de Infeções Puerperais.** By J. Coriolano de Carvalho, Premio Alvarenga da Faculdade Nacional de Medicina. 40 pages. Trabalho apresentado e discutido na 11 Semana Paulista-Carioca de Ginecologia e Obstetrica, de Setembro de 1943. Rio de Janeiro. 1943.

[18]**Pain Mechanisms.** A Physiologic Interpretation of Causalgia and Its Related States. By W. K. Livingston, Lieutenant Commander, (MC), USNR. Pp: 248. The Macmillan Company, New York, 1943.

clinicians. The material deals, first, with the physiology and psychology of pain; second, with the clinical aspects, and finally, with the interpretation. Some chapters of the book, chronic low back disability, the sympathetic component, and the vicious circle, would be of interest to many gynecologists as an aid in the solution of some traumatic or sympathetic system disorders, which not infrequently, appear in their practices. To the surgeon or neuropsychiatrist who will handle many cases of this type after the war, this book should be of much value.

PHILIP F. WILLIAMS.

After eight years, a second translation of Hermann Zondek's **The Diseases of the Endocrine Glands** by Carl Prausnitz Giles,[19] a translation of the fourth German edition, has appeared. This is a book based upon a large clinical experience, deeply tinged by the author's personal views, often therefore interesting and illuminating, but sometimes distinctly hypothetical. The book is designed for clinicians.

The introductory chapters dealing with the physiology of the hormones and the individual glands are very clear, detailed and informative. The chapters on diseases of the thyroid are good; those describing the pituitary disturbances are excellent. Obesity is gone into fully. On the other hand, only ten pages are devoted to adrenal diseases and hyperinsulinism is given only five pages. Diabetes has not been included. Most of the remainder of the volume is devoted to disorders of the generative system—both male and female—considered from many aspects, including their effect on tumor formation, blood, etc. Therapy is described in great detail and without undue overoptimism. The illustrations are numerous and original. The translation is excellent and smooth.

R. T. FRANK.

According to the publisher's preface, **Sexual Anomalies**[20] was written by the pupils of Magnus Hirschfeld, based upon his notes as well as his published papers. Hirschfeld had planned to write this book himself. The names of none of these pupils appear in the volume. The book is designed for those whose professional duties require a knowledge of sexual pathology—physicians, criminologists, attorneys, judges, probation officers and educators.

In the early years of this century, Hirschfeld played a dominant role in this field throughout the Germanic countries. He founded and endowed an institute for Sexualwissenschaft in Berlin, and then presented it to the German people. With the advent of the Nazis, the institute was discontinued, the author's books publicly burned, as well as his notes and huge number of case histories.

In the present textbook, Hirschfeld and his pupils have essayed to combine the developmental, hormonal and Freudian theories in a concise, readable form. The main bulk of the volume consists of numerous case histories.

R. T. FRANK.

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[19]**The Diseases of the Endocrine Glands.** By Hermann Zondek, M.D. (Berlin). Director of the Medical Division, Bikur Cholim Hospital, Jerusalem; Late Extraordinary Professor of Medicine in the University of Berlin and Director of the Medical Division of the Krankenhaus am Urban in Berlin; late Honorary Physician to the Victoria Memorial Jewish Hospital, Manchester. Fourth (Second English) Edition. Translated by Carl Prausnitz Giles, M.D. (Breslau), M.R.C.S. (Eng.), L.U.C.P. (Lond.). Late Honorary Research Fellow, Victoria University of Manchester; Late Professor of Hygiene and Bacteriology, University of Breslau. 496 pages. Williams & Wilkins Company, Baltimore. 1944.

[20]**Sexual Anomalies and Perversions.** Physical and Psychological Development and Treatment. A Summary of the Works of the Late Professor Dr. Magnus Hirschfeld, President of the World League for Sexual Reform, Director of the Institute for Sexual Research, Berlin, etc. Compiled as a Humble Memorial by his Pupils. 630 pages. Francis Aldor Publisher, London, England. Emerson Books, Inc., New York. 1944.

From its initial chapter on historical consideration, to the concluding, very timely chapter on **Intravenous Anesthesia,**[21] in Military Surgery, this monograph discusses exhaustively a technique which is assuming increasing importance in the field of anesthesiology and surgery. Individual chapters are allotted to all the drugs that have been employed for anesthesia by this method. Following a historical survey, the chemistry, pharmacology, clinical use, indications and contraindications for administration of these agents, are discussed in detail. A complete bibliography is included in each chapter. The technique of administration is described thoroughly by the text and by numerous illustrations.

Special consideration is given to pentothal sodium, which to the present time, has proved to be the most satisfactory drug for intravenous anesthesia. The author's very extensive personal experience in the use of this drug makes this chapter particularly valuable. This is an informative book for the anesthetist student and research worker.

BERNARD H. ELIASBERG.

This volume **The Art of Anesthesia**[22] carries but very inconsequential changes in the text of the previous edition. There has been added a chapter on Fire Hazard in Anesthesia, a chapter on Our Wives and Children—Who Shall Anesthetize Them? a very short chapter on Continuous Spinal Anesthesia, and a concluding, very brief chapter on Continuous Caudal Anesthesia in Obstetrics. Its popularity is attested to by the fact that it has undergone seven editions.

BERNARD H. ELIASBERG.

The fifth edition of **Hewer's Recent Advances in Anaesthesia and Analgesia**[23] has appeared in twelve years. This is not surprising because the book contains a large amount of information in small compass.

In spite of the pressure of war, research in anesthesia has not lagged, in fact it has been stimulated in certain fields. The new edition contains additions on anesthesia for thymectomy (myasthenia gravis), intravenous general analgesia with ethyl chloride, trichlorethyline and procaine, analgesia in obstetrics, fractional caudal block, etc. Concise chapter bibliographies and liberal illustrations add to the value and readability of the book.

R. T. FRANK.

Minor Surgery,[24] edited by Rolleston and Moncrieff, contains eighteen contributions by as many authors on diverse subjects—minor wounds, sprains, the feet, the hand, the mouth, the nose and throat, the ear, the eye, bursae and ganglia, some benign tumors and cysts, skin infections, the rectum, the genitourinary system, nonoperative treatment of hernia, varicose veins, ulcers and phlebitis, gynecology, childhood, and anesthesia and analgesia.

There is no preface or introduction, but from the text one gathers the impression that this small volume is designed for ready reference especially for the

[21] **Intravenous Anesthesia.** By R. Charles Adams, M.D., C.M., M.S., Associate in Section on Anesthesiology, Mayo Clinic, Rochester, Minn. Cloth. Pp. 663, with 75 illustrations. New York and London. Paul B. Hoeber, Inc., 1944.

[22] **The Art of Anesthesia.** By Paluel J. Flagg, M.D. Visiting Anesthestist to Manhattan Eye and Ear Hospital, New York City, Seventh Edition. Cloth. Pp. 519, with 166 illustrations, and foreword by Dr. Rudolph Matas. Philadelphia. J. B. Lippincott Co. 1944.

[23] **Recent Advances in Anaesthesia and Analgesia (Including Oxygen Therapy)** by C. Langton Hewer, M.D., B.S. (Lond.), D.A. (Eng.). Senior Anaesthetist, St. Bartholomew's Hospital and St. Andrew's Hospital, Dollis Hill; Anaesthetist, Brompton Chest Hospital and Emergency Medical Service, etc. Fifth Edition with 141 illustrations. 343 pages. The Blakiston Company, Philadelphia. 1944.

[24] **Minor Surgery.** Edited by Humphry Rolleston and Alan Moncrieff. 174 pages. Philosophical Library, New York. 1944.

practitioner, who must be prepared to cope with all situations often under wartime conditions. However, the content is not limited to acute or traumatic disturbances.

For disinfection of minor wounds Dettol is recommended. Varicose veins are injected with quinine and urethane. The chapter on gynecology was contributed by Douglas MacLeod. It includes Bartholinian conditions, urethral caruncle, episiotomy, perineal and vaginal lacerations, cervical polyps, trachelorrhaphy, amputation of the cervix, cervical dilatation, curettage, insufflation and visualization of the tubes. That the advice is designed for action under wartime conditions is evidenced by the advice for treatment of complete perineal tears—"Should the delivery occur at night, it is wise to wait until the following day in order to have sufficient light and assistance at its performance."

The text is concise and authoritative.

R. T. FRANK.

A monograph by Ribeiro on **Lithiasis of the Appendix**[25] contrasts the frequency of coproliths and the rarity of true appendicular stone. A coprolith is a fecal concretion; a stone usually consists of a fecal core about which mineral salts have formed layers. During its formation stones remain clinically quiescent, but eventually may produce an acute appendicitis.

The author reports one case, the appendix containing four stones. Complete literature.

R. T. FRANK.

Chronology of the Evolution of Plastic Surgery[26] is in the nature of a prospectus of a book to appear next year by the same author and publishers, a chronology which covers the periods from the first century B.C. to 1944, in the form of a thirty-two-page pamphlet. It begins with the Chinese tannic acid treatment of burns five thousand years B.C., and ends with an osteoplastic procedure for funnel chest. For quick reference it might be of value.

R. T. FRANK.

This book[27] represents, in large part, a summary of the studies made by these authors in hypertensive diseases by measurements of the effective renal blood flow, filtration rate and maximal tubular excretory capacity with the diodrast and inulin methods devised by Homer Smith. There are excellent chapters on the clinical aspects of hypertensive diseases, on systemic hemodynamic alterations in hypertension, and renal functional and renal hemodynamic alterations in hypertension. They repeat the often quoted statement that "the cause of essential hypertension is unknown." While this is true as far as the precise mechanism is concerned, one cannot ignore the abundant accumulated evidence of the psychogenic origin of essential hypertension. Indeed, the authors emphasize the value of psychotherapy in the therapy, but aside from this brief comment there is no

[25] **Litíase do Apêndice.** By Eurico Branco Ribeiro, Director Do Sanatório São Lucas. 87 pages. Sociedade Editora Médica Limitada, São Paulo, Brazil. 1943.

[26] **Chronology of the Evolution of Plastic Surgery.** By Maxwell Maltz, B.S., M.D., Sc.D., F.I.C.S.; Director, Department of Plastic and Reconstructive Surgery, West Side Hospital and Dispensary; Honorary Professor of Surgery, Universities of Santo Domingo, Nicaraugua, Honduras, San Salvador, Guatemala, etc. This Chronology is a section from the author's volume: The Evolution of Plastic Surgery (Froben Press, 1945). 32 Pages. Froben Press, New York. 1944.

[27] **Hypertension and Hypertensive Disease.** By William Goldring, Associate Professor of Medicine, New York University College of Medicine; Chief, Nephritis and Hypertension Clinic, New York University Clinic; Physician to the Adult Cardiac Clinic and Associate Visiting Physician, Third (New York University) Medical Division, Bellevue Hospital; Visiting Physician, Goldwater Memorial Hospital, and Herbert Chasis, Assistant Professor of Medicine, New York University College of Medicine; Associate Chief, Nephritis and Hypertension Clinic, New York University Clinic; Physician to the Adult Cardiac Clinic and Assistant Visiting Physician, Third (New York University) Medical Division, Bellevue Hospital; Cardiologist to the French Hospital, New York, The Commonwealth Fund, 1944.

discussion of this important phase of the etiology of essential hypertension. They conclude that the results attained by experimental hypertension cannot be applied to human hypertension except to a very limited degree, and that there is no proof that essential hypertension is of primary renal origin. They are skeptical of the reports of the cure of hypertension by unilateral nephrectomy. There are two long chapters on therapy of hypertensive disease. They do not approve of the thiocyanate treatment and conclude that renal extracts have thus far been unsuccessful in the treatment of hypertension. The principal effect of sympathectomy is the relief of subjective symptoms, and the occasional temporary reduction of blood pressure to lower levels.

The work concludes with several appendices on methodology of blood pressure measurement with the direct method; cardiac output measurement; peripheral resistance; the rate of glomerular filtration, effective renal plasma flow, maximal tubular excretory capacity, maximal tubular resorptive capacity; composite kidney function test, functional and hemadynamic measurements of separate kidneys and a presentation and discussion of renal functional data in hypertensive patients. One misses a chapter on the anatomical aspects of hypertension. The authors omitted it because these may be found in other books, but this argument may be applied to a large part of the text of this volume; a clear perspective of hypertensive disease can hardly be gained without including a background in morbid anatomy. Within its scope, this book is excellent and informative.

ELI MOSCHCOWITZ.

The Twentieth Edition of Dorland's Medical Dictionary[28] covers every department of medicine and surgery and the allied fields. The many additions and alterations required to meet recent advances have necessitated a complete revision of previous editions. The *Standard Nomenclature of Diseases and Operations* has been used as the basis of terminology and constitutes a notable feature. Attention may also be called to the gallery of portraits of eminent medical men and their principal association with accepted terms. Perhaps in later editions, the insertion of a few more biographic details might be considered. The various tabulations are also of importance. The collaboration of Dr. E. C. L. Miller, well-known librarian of the Medical College of Virginia, is an important addition to the list of other competent authorities in their respective fields, making this new edition the outstanding work of reference in American medical literature.

GEORGE W. KOSMAK.

This **Golden Book**[29] is an anniversary volume dedicated to Professor Osvaldo L. Bottaro upon the completion of thirty years of professorship including his gynecologic service at the Hospital San Roque (1912-____). The recipient of this honor has published over many years diverse subjects in gynecology and obstetrics, as well as on public health problems.

The content of this faultlessly gotten up volume of nearly five hundred pages does not lend itself to detailed review as it embraces every aspect of medicine including such diverse subjects, selected at random, as the medical, ethical and professional aspects of female sterility, the treatment of tuberculous cavities, postoperative exophthalmos in Basedow's disease, recent advances in the therapy of mental diseases, in addition to a number of strictly gynecologic themes.

R. T. FRANK.

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[28]**The American Illustrated Medical Dictionary.** By W. A. Newman Dorland, A.M., M.D., F.A.C.S., Twentieth Edition. Revised and Enlarged. With the Collaboration of E. C. L. Miller, M.D., Philadelphia and London, W. B. Saunders Co., 1944. 1668 pages. Price $7.00, thumb-indexed, $7.50.

[29]**Libro de Oro.** Ofrecido Al Professor Honorario Dr. Osvaldo L. Bottaro. Al Cumplir 30 Años en el Ejercicio Del Profesorado por sus Discipulos, Colaboradores y Amigos. 493 pages. Alfredo Frascoli, Buenos Aires. 1943.

Item

American Board of Obstetrics and Gynecology

Examination

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Saturday, February 3, 1945, at 2:00 P.M.

Arrangements will be made so far as is possible for candidates in Military Service to take the Part I examination (written paper and submission of case records) at their places of duty, the written examination to be proctored by the Commanding Officer (medical) or some responsible person designated by him. Material for the written examination will be sent to the proctor several weeks in advance of the examination date. Candidates for the February 3, 1945, Part I examination, who are entering Military Service, or who are now in Service and may be assigned to foreign duty, may submit their case records in advance of the above date, by forwarding the records to the Office of the Board Secretary. All other candidates should present their case records to the examiner at the time and place of taking the written examination.

The Office of the Surgeon General (U. S. Army) has issued instructions that men in Service, eligible for Board examinations, be encouraged to apply and that they may request orders to Detached Duty for the purpose of taking these examinations whenever possible.

All candidates will be required to take both the Part I examination, and the Part II examination (oral-clinical and pathology examination). Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held later in the year.

Notice of the exact time and place of the Part II examinations will be sent all candidates well in advance of the examination date. Candidates in Military or Naval Service are requested to keep the Secretary's Office informed of any change in address.

If a candidate in Service finds it impossible to proceed with the examinations of the Board, deferment without time penalty will be granted under a waiver of our published regulations applying to civilian candidates.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

PAUL TITUS.

Necrology

Elijah White Titus

Elijah White Titus, M.D., a graduate of George Washington University, in 1910, Clinical Professor in Obstetrics and Gynecology in the latter, Attending Gynecologist in the Columbia Hospital for Women and the George Washington University Hospital, Fellow of the American College of Surgeons, Past President of the Washington Medical Society, a diplomate of the Board of Obstetrics and Gynecology, died at his home, in Washington, D. C., December 11, 1944, after a brief illness.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President,* Edward A. Schumann, Philadelphia, Pa. *Secretary,* Howard C. Taylor, Jr. 842 Park Ave., New York, N. Y. Next annual meeting, June, 1945.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* Lewis F. Smead, Toledo, Ohio. *Secretary,* James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 1944.

Central Association of Obstetricians and Gynecologists. (1929) *President,* John H. Moore, Grand Forks, N. D. *Secretary-Treasurer,* W. F. Mengert, Dallas, Tex. Annual meeting not announced.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President* Oren Moore, Charlotte, N. C. *Secretary,* T. J. Williams, University, Va. Annual meeting cancelled.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Philip F. Williams, Philadelphia, Pa. *Secretary,* William Mengert, 2211 Oak Lawn Ave., Dallax Tex. Next meeting, Philadelphia, Pa., June 18-22, 1945.

New York Obstetrical Society. (1863) *President,* W. E. Studdiford. *Secretary,* R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. (1868) *President,* Charles A. Behney *Secretary,* John B. Montgomery, Pro tem, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President,* William J. Dieckmann. *Secretary,* Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President* Chas W. Mueller. *Secretary,* William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. (1929) *President,* Lawrence Wharton. *Secretary-Treasurer,* John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. *President,* Edward Friedman. *Secretary,* Carroll J. Fairo, Cincinnati, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Layman A. Gray. *Secretary,* E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Howard Stearns. *Secretary,* William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* H. A. Power. *Secretary,* Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.

Obstetrical Society of Boston. (1861) *President,* Thos. Almy, Fall River, Mass. *Secretary,* Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the name is the year of founding.

New England Obstetrical and Gynecological Society. (1929) *President,* Roy J. Hefferman, Brookline, Mass. *Secretary,* Fred J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* T. Floyd Bell. *Secretary-Treasurer,* William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.

Washington Gynecological Society. (1933) *President,* James R. Costello. *Secretary,* J. Keith Cromer, 1835 Eye St., N.W., Washington, D. C. Fourth Saturday, October to May.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* E. L. Zander. *Secretary,* R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.

St. Louis Gynecological Society. (1924) *President,* S. A. Weintraub. *Secretary,* Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President,* R. Glenn Craig. *Secretary,* D. G. Morton, California University Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* T. F. Bunkley. *Secretary,* J. McIver, 714 Medical Arts Bldg., Dallas, Tex.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President,* Norman F. Miller. *Secretary,* Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Obstetric Society of Syracuse Hospitals. (1938) *President,* Edward C. Hughes. *Secretary,* Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May. Suspended for the duration.

Alabama Association of Obstetricians and Gynecologists. *President,* J. M. Weldon, Mobile, Ala. *Secretary,* Eva F. Dodge, Montgomery, Ala.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President,* R. Philip Smith. *Secretary,* Gerhard Ahnquist, 1336 Madison Street, Seattle. Meetings held on third Wednesday of each month.

Denver Obstetrical and Gynecological Society. (1942) *Secretary,* Emmett A. Mechler, 1612 Tremont St., Denver, Colo. Suspended during war.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* Roland S. Cron. *Secretary,* Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President,* Geo. D. Huff. *Secretary,* Frank Russell, 233 A St., San Diego, Calif. Meetings held on the last Wednesday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Ralph E. Leigh, Grand Forks. *Secretary,* G. Wilson Hunter, 807 Broadway, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President,* A. L. Carson, Jr. *Secretary,* L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.